

## UNITED STATES AIR FORCE RESEARCH LABORATORY

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### CARDIORESPIRATORY AND PERFORMANCE RESPONSES TO SUSTAINED PRESSURE BREATHING

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## **ABSTRACT:**

Positive pressure breathing (PPB) is used to provide pilot life support during cockpit depressurization at altitudes at which the ambient pressure is insufficiently high to maintain adequate oxygen tension even when breathing 100% O<sub>2</sub>. Although pulmonary barotrauma and hypotension can usually be prevented by an external chest counterpressure jerkin and a G-suit, involuntary hyperpnea, presumably caused by activation of an upper airway stretch receptor, can limit pilot performance. This phenomenon was investigated in 10 normal volunteers wearing the COMBAT EDGE, who were instrumented to obtain arterial blood samples while different forms of applying positive pressure breathing were applied. In order to study effects on cardiac output, four subjects were instrumented with pulmonary artery catheters while they breathed 34% O<sub>2</sub> at a simulated altitude of 24,900 ft in a hypobaric chamber, in order to simulate 100% O<sub>2</sub> breathing at 50,000 feet. Psychomotor performance was assessed using a subset of the Tri-Service Cognitive Battery implemented on a laptop computer.

Phasic pressure support with greater pressure during expiration (expired positive airway pressure: EPAP) was intolerable to subjects because of an extremely high work of breathing. Compared with conventional PPB, phasic pressure support during inspiration tended to increase ventilation, as demonstrated by lower arterial PCO<sub>2</sub>.

Oscillatory pressure changes at 6-12 Hz superimposed upon constant PPB using the COMBAT EDGE did not reflexly inhibit the usually observed involuntary hyperventilation. Hypocapnia could be avoided by adding CO<sub>2</sub> to the inspired gas.

A fundamental determinant of subject psychomotor performance in this study was arterial PCO<sub>2</sub>. Hypocapnia induced by involuntary hyperventilation impaired psychomotor performance when arterial PCO<sub>2</sub> values fell below 20 mmHg. Within the range of inspired PO<sub>2</sub> values to which these subjects were exposed (arterial PO<sub>2</sub> range 52-181 mmHg), there was no effect of arterial PO<sub>2</sub> on the measures of performance used in this study.

There was a significant difference between end-tidal and arterial PCO<sub>2</sub>, with end-tidal values tending to underestimate arterial CO<sub>2</sub> tension by up to 25 mmHg.

Impairment of psychomotor performance due to hypocapnia during PPB at a simulated altitude of 50,000 ft (24,900 ft chamber altitude, 34% O<sub>2</sub>) can be prevented by the addition of CO<sub>2</sub> to the breathing gas.

## **INTRODUCTION:**

The Combat Edge life support system utilizes assisted positive pressure breathing (PPB with chest counterpressure) to provide aviators with increased protection from the physiological hazards associated with flying high performance aircraft at high altitudes. Raising the pressure of the breathing circuit throughout the breathing cycle (PPB) is a well established method of maintaining alveolar oxygen tension at high altitudes and high G-forces.

Sustained PPB at levels of 60 mmHg pressure can have detrimental effects, including significant changes in cardiopulmonary function. These include decreases in cardiac output, reflex hyperventilation with resultant hypocapnia, alteration in  $V_A/Q$  matching and possible respiratory muscle fatigue. The mechanism of reduction in cardiac output has not been elucidated, though it is probably at least in part due to redistribution of central blood volume to the periphery, increase in pulmonary vascular resistance (due to high alveolar pressure) and shift in the cardiac inter-ventricular septum toward the left. The resulting hypotension and hypocapnia (and presumed reduction in cerebral blood flow) likely impair pilot performance.

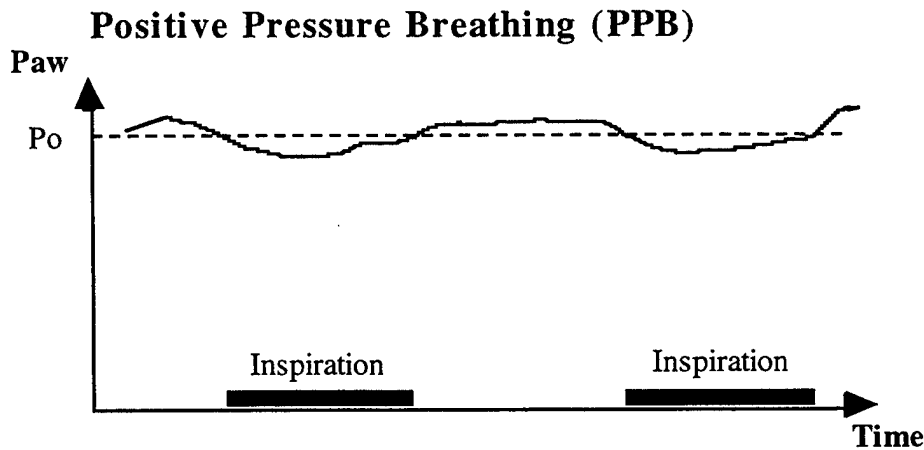
Diminished cardiac output and inability to sustain arterial pressure during periods of high level PPB has been shown in part to be alleviated by G-suit inflation to a pressure three to four times the breathing pressure with full coverage lower extremity suits providing greater cardiovascular support than partial coverage G-suits. Phasic swings in mask pressure also seem to augment venous return and enable subjects to maintain mean arterial pressures at sustained PPB levels to 60 mmHg, especially under simulated altitude conditions (low breathing gas density/high gas compressibility). These effects have not been systematically studied in conjunction with invasive arterial gas studies which are necessary due to the discrepancy between end-tidal and arterial carbon dioxide ( $CO_2$ ) and oxygen ( $O_2$ ) tensions under these conditions.

It has been suggested that altered patterns of breathing, or assisted breathing, might enhance venous return and allow both  $PaO_2$  and cardiorespiratory function to be maintained within acceptable limits during high level PPB. Previous attempts to use assisted breathing resulted in excessive hyperventilation. However, in those studies, because of technological limitations, the timing of the breaths, rather than being under the control of the subjects' respiratory control center, was arbitrary.

The involuntary hyperventilation which accompanies PPB results in a beneficial elevation of arterial  $PO_2$ , which tends to extend altitude tolerance. However, the accompanying hypocapnia (arterial  $PCO_2$  lower than 25-30 mmHg) causes cerebral vasoconstriction and at extremely low values may lead to altered neuromuscular functioning (tetany) and loss of consciousness. While excessive hyperventilation during pressure breathing is detrimental, even with extreme voluntary effort by experienced subjects it is difficult or

impossible to prevent. Its mechanism is unknown, though it is evident that it is not merely compensatory for an increase in dead space and high  $V_A/Q$  lung units (lung units with high ventilation to perfusion ratios). We undertook this study to investigate whether application of phasic breathing pattern interventions during simulated high altitude hypoxic conditions would allow maintenance of oxygenation, cardiovascular function and cognitive performance at lower levels of PPB while also resulting in less of a reflex hyperventilation. We further postulated that the normalization of  $PaCO_2$  by the addition of carbon dioxide to the inspired gas mixture during PPB at altitude would improve both  $PaO_2$  and neurocognitive performance.

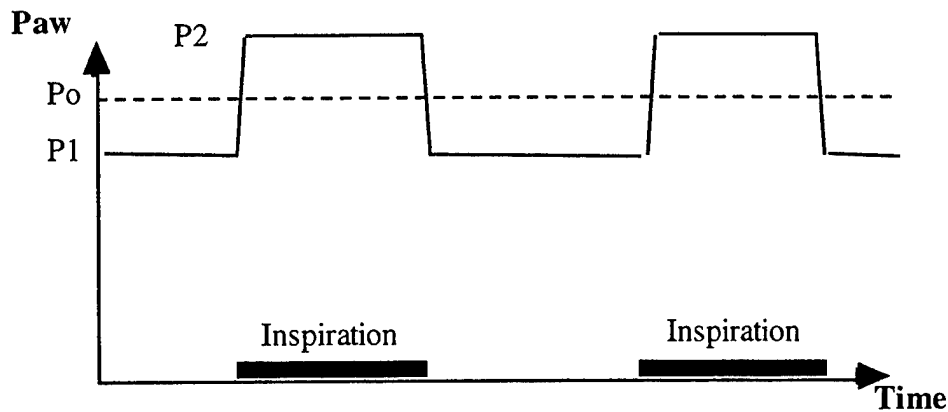
Phasic and oscillatory pressure manipulations are shown in Figs. 1-4. Airway pressure ( $P_{aw}$ ) throughout the breathing cycle is plotted as a solid line as a function of time. The broken line at  $P_0$  is mean  $P_{aw}$  and represents the underlying mean PPB. Inspiratory cycles are depicted along the abscissa.



Positive Pressure Breathing (PPB) is similar to clinical Continuous Positive Airway Pressure (CPAP). This is the standard respiratory support provided by the COMBAT EDGE system. Mean airway pressures ( $P_0$ ) are maintained throughout the respiratory cycle at a predetermined  $P_0$  target pressure (30 or 60 mmHg). Inspiratory and expiratory pressures are both positive, although the inspiratory is less than the expiratory.

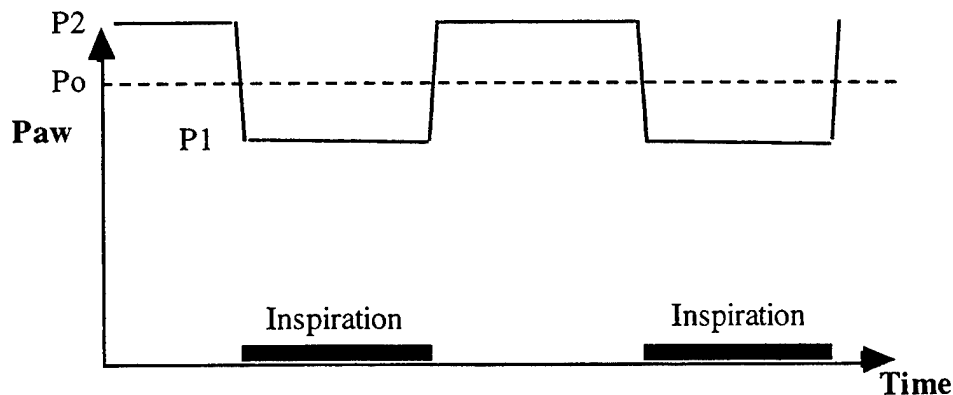


### Inspiratory Pressure Support



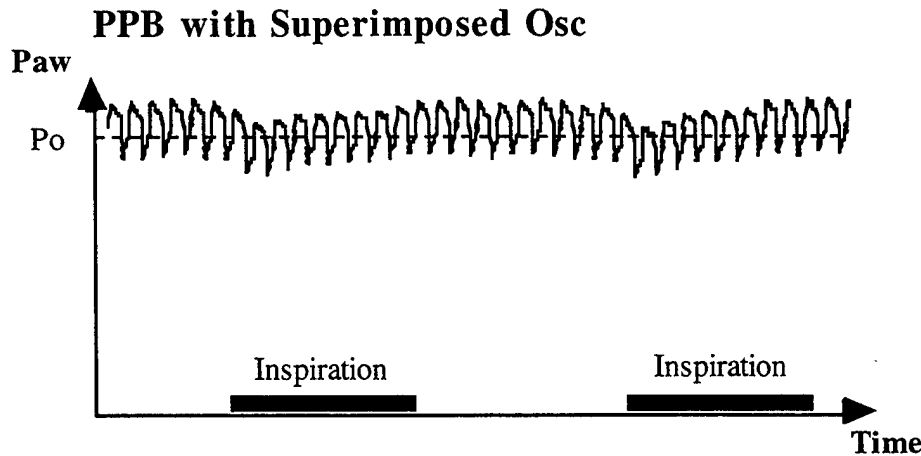
During Inspiratory Pressure Support ventilation (PS), inspiratory effort is augmented by a predetermined amount of pressure support. The ventilator is subject-triggered "ON", and continues in the inhalation phase to a preselected positive-pressure limit. As long as the inspiratory flow is maintained, the preselected airway pressure stays constant, with a variable flow rate of gas from the ventilator. Inhalation cycles "OFF" when the subject's inspiratory flow decreases to a predetermined value, and passive exhalation then occurs. In the modified Bear 1000 ventilator used for this experiment, the exhalation pressure was determined by the level of PPB or CPAP. The baseline PPB ( $P_1$ ) was set to 50 mmHg and the augmentation of inspiration was set to 20 mmHg ( $P_2 = 70$  mmHg;  $P_2 - P_1 = 20$  mmHg), Mean airway pressure ( $P_0$ ) was held at 60 mmHg.

### Expiratory Phase Increase (EPAP)



Expiratory effort is enhanced during Expiratory Positive Airway Pressure (EPAP) interventions. The expiratory pressure limit is set to 70 mmHg ( $P_2$ ) during a baseline

PPB (CPAP) of 50 mmHg (P1). Mean airway pressures are maintained at 60 mmHg (P0).



High frequency pressure oscillations (6 Hz or 12 Hz) administered throughout the breathing cycle around mean airway pressures of 60 mmHg (P0). Peak to peak pressure swings ranged from 55 mmHg to 65 mmHg.

We hypothesized the following:

- (1) Phasic pressure support would be superior to constant PPB using the COMBAT EDGE with ATAGS by allowing greater venous return, and hence higher blood pressure and cardiac output.
- (2) Oscillatory pressure changes superimposed upon constant PPB using the COMBAT EDGE would reflexly inhibit the usually observed involuntary hyperventilation.
- (3) Hypocapnia induced by involuntary hyperventilation would impair psychomotor performance as measured by a standard neurocognitive test battery.
- (4) The addition of carbon dioxide to the inspired gas mixture during PPB at 60 mmHg, in addition to raising alveolar  $PO_2$ , can normalize  $PaCO_2$  and improve neurocognitive performance.
- (5) End-tidal  $PCO_2$ , the conventionally used, non-invasive assessment of arterial  $PCO_2$ , would significantly underestimate arterial  $PCO_2$  during PPB.

## **METHODS:**

### **Selection of Subjects:**

After obtaining institutional approval, 10 healthy volunteers (7 male, 3 female) were selected for the study. Anthropometric data are summarized below in Table 1. Age ranged from 19 to 35 years old (mean 27.6 years). All lived near Durham, NC (elevation 460 ft.). Subjects underwent physical examination and were screened for gross obesity, history of cardiopulmonary disease and pregnancy (serum  $\beta$ HCG, females). All subjects had normal posterior-anterior and lateral chest radiographs, normal 12-lead EKG's, normal spirometry and lung volumes, and normal resting arterial blood gases. Each subject was briefed on the risks of positive pressure breathing and high altitude exposure and the risks of pulmonary artery catheterization. Subjects unfamiliar with pulmonary artery catheterization watched a videotape demonstrating the procedure. Consent was obtained in accordance with the guidelines of the Duke University Institutional Review Board for Human Experimentation (Protocol #1582-95-11: consent form appended).

### **Training:**

Subjects were fitted to a standard issue Air Force COMBAT EDGE life support system. This apparatus consists of a tightly fitting face mask and helmet, a chest counter pressure vest to prevent pulmonary overexpansion and a full coverage inflatable lower extremity garment (ATAGS) designed to prevent peripheral blood pooling during administration of PPB. Subjects underwent several training sessions on this apparatus at PPB of 30 mmHg without leg or chest counterpressure, and at PPB of 60 mmHg with chest counterpressure of 60 mmHg and leg counterpressure of 60 and 180 mmHg until they demonstrated the ability to comfortably maintain steady state ventilation for five minutes. As an additional safety measure, subjects were instructed on how to break the mask pressure seal by jaw movement in case they felt overwhelmed by the pressure.

Additional training was also provided for the Pressure Support (PS) mode of ventilatory support, oscillatory ventilation (Osc) superimposed on PPB of 60 mmHg, and EPAP of 60 mmHg (see below). Subjects randomly practiced each mode of ventilatory intervention until they demonstrated their comfort with the various modes and their ability to maintain steady state ventilation without mask leak for a minimum of 5 minutes.

Table 1: Anthropometric and Pulmonary Function Data

	Age (y)	Sex	Ht (cm)	Wt (kg)	FVC (L BTPS)	% Pred	FEV <sub>1</sub> (L BTPS)	% Pred	FEV <sub>1</sub> /FVC	FEF <sub>25-75</sub> (L BTPS)	% Pred
BA	22	M	185	86	5.41	95.2	4.25	86.6	0.79	3.98	73.1
DH	33	F	170	62	4.03	99.4	3.46	101.8	0.86	3.87	109.1
FC	35	M	188	105	5.90	100.3	4.43	93.3	0.75	4.91	96.4
GH	22	M	184	70	6.01	107.2	4.84	100.1	0.81	4.29	79.9
MB	27	F	173	80	3.84	89.3	3.04	83.5	0.79	2.83	74.2
MH	29	M	175	73	4.61	87.8	3.89	89.2	0.84	4.11	89.8
NH	19	F	175	62	3.82	91.5	3.50	101.4	0.92	4.78	105.8
RB	29	M	185	77	5.05	86.3	3.79	79.3	0.75	2.94	56.8
SA	30	M	178	105	5.58	103.9	4.32	97.2	0.77	3.67	78.3
TW	30	M	184	83	6.05	105.0	4.99	106.0	0.82	5.40	106.7
Mean	27.6		179.7	80.3	5.03	96.6	4.05	93.8	0.81	4.08	87.0
SD	5.13		6.22	15.27	0.90	7.62	0.63	8.89	0.05	0.82	17.39
95% CI	3.18		3.85	9.47	0.56	4.72	0.39	5.51	0.03	0.51	10.78
Low	19		170	62	3.8	86.3	3.04	79.3	0.75	2.83	56.8
High	35		188	105	6.1	107.2	4.99	106.0	0.92	5.40	109.1

## **Experimental Set Up**

Control studies for PPB, pressure support, oscillatory ventilation, and EPAP under normobaric conditions were performed in the human physiology lab at the F.G. Hall Environmental Laboratory, Duke University Medical Center. The subject was seated in a semi-reclined position to simulate the position of the pilot in an F-16 during flight. The CRU-93 pressure demand regulator supplied gas to the breathing mask. The chest counterpressure vest and anti-G suit pressures were independently regulated to 0, 60 or 180 mmHg by a separate regulator as per the experimental protocol (Table 2, Experimental Protocol, below). Expired gas was collected in a Douglas bag for volumetric determination with a calibrated dry gasometer (American Meter Company DTM 325-4, Nebraska City, NE). The bag was emptied to a standard pressure of negative 5 cm of water that was regulated through a pop-off valve on the gasometer. The subject was instrumented with an arterial catheter and for EKG (see text). Breathing parameters and physiological signals were connected to an A/D converter and then to a digital computer for data storage and analysis as described below.

Ground level studies of gas exchange and neurocognitive performance with normocapnia during PPB of 60 mmHg were performed by having the volunteers breathe pre-mixed gas containing carbon dioxide. Inspired carbon dioxide ranged from 2% to 4% and was chosen based on previous experience with rebreathing and PPB studies. Subjects RB, NH, GH, and MH achieved normocapneic ventilation with the 2% inspired CO<sub>2</sub> while MB, SA, and BA breathed the 4% inspired gas.

The choice of inspired carbon dioxide tension at 24,900 ft. was based on metabolic measurements obtained from previous experiments on volunteers breathing PPB of 60 mmHg at both ground level and 24,900 ft. simulated altitude (barometric pressure 283 mmHg). After analysis of sea level data for eucapnia and normocapnia with PPB, four conditions and rest were selected to be performed at a simulated altitude of 24,900 ft. breathing a pre-mixed gas containing 34% inspired oxygen with and without 10% inspired CO<sub>2</sub>, balance nitrogen. This gas mixture was chosen by using the alveolar gas equation to estimate the alveolar (and therefore arterial) oxygen tensions for subjects hyperventilating to a PaCO<sub>2</sub> of 20 mmHg at 50,000 ft. on 100% oxygen with a PPB of 60 mmHg and with a respiratory quotient of 1.3. The alveolar gas equation is described below. After the first experimental altitude exposure the inspired breathing gas was changed from 34% to 30% inspired oxygen as the assumptions used in the prediction equation seemed to underestimate actual PaO<sub>2</sub>. The inspired concentrations of carbon dioxide remained at 10%. Tables 3-8 on pages 60-66 show the theoretical effects of changes in the various parameters in the prediction equation on P<sub>A</sub>O<sub>2</sub> at altitude as calculated above.

Alveolar Gas Equation:

$$PAO_2 = \frac{P_I O_2 R + PACO_2 F_I O_2 (1 - R) + P_I CO_2 - PACO_2}{F_I CO_2 (1 - R) + R}$$

where  $PAO_2$ ,  $PACO_2$  = alveolar  $PO_2$ ,  $PCO_2$ ;  $F_I O_2$ ,  $F_I CO_2$  = inspired  $O_2$ ,  $CO_2$  concentrations;  $P_I O_2 = F_I O_2 (P_{\text{barometric}} - PH_2O)$ ;  $P_I CO_2 = F_I CO_2 (P_{\text{barometric}} - PH_2O)$ .  $P_{\text{barometric}}$  was corrected to account for the effects of PPB pressure on gas tensions in the alveoli. The respiratory exchange ratio (R) is defined as the ratio of  $CO_2$  production to  $O_2$  consumption and can be expressed by the following equation:

$$R = \frac{F_E CO_2 - F_I CO_2 (F_E N_2 / F_I N_2)}{F_I O_2 (F_E N_2 / F_I N_2) - F_E O_2}$$

where  $F_I N_2$ ,  $F_E N_2$  are the inspired and mixed expired nitrogen concentrations. Four subjects participated in altitude exposures in "F" chamber at the FG Hall Environmental Center utilizing the same experimental set up as for surface controls. A pulmonary artery catheter was additionally placed for these studies. Analog outputs from the physiological monitors were connected to the 8 channel A/D converter via through-hull penetrators. Chamber pressure was monitored with a model 370 digital pressure gauge (Setra Systems, Acton, MA) and a model 65C-1G-2002X differential pressure gauge (Wallace and Tiernan, Belleville, NJ).

*Breathing Circuit:* The COMBAT EDGE manside test kit supplied by the USAF was connected to a high-volume regulator set between 80 and 100 psig. Breathing gas for all PPB experiments was delivered to the oronasal mask from the CRU-93 pressure demand regulator via a chest-mounted manifold (CRU-94/P Integrated Terminal Block or ITB). In addition, regulated gas was supplied to bladders located in the flight helmet as an assist in maintaining a tight mask seal. During PPB at 60 mmHg, gas was also delivered at 60 mmHg from the regulator to the chest counterpressure vest via the ITB. Breathing gas pressures and inflation of the ATAGS G-suit (through independent regulators) was according to the experimental protocol outlined in Table 2 and depicted in Figure 1. PPB was altered with PS and EPAP over the baseline PPB level to a predetermined average airway pressure as described below.

Inspiratory Pressure Support ventilation (PS) was achieved by connecting a modified Bear 1000 ventilator (Bear Medical Systems, Inc., San Anselmo, CA) to the inspiratory valve of the aviator mask. The high pressure ventilator alarms were disconnected and the flow restrictor to the jet pump, designed to prevent overpressurization, was bypassed. This allowed pressure support ventilation at mean airway pressures of 60 mmHg. The ventilator was set to a CPAP (continuous positive airway pressure) of 50 mmHg with a pressure support of 20 mmHg, a pressure slope of 5 (rate at which the ventilator pressure support level is reached, arbitrary units) and a trigger sensitivity of 5 cmH<sub>2</sub>O, such that mean airway pressure was maintained at 60 mmHg (Figure 2). The chest counterpressure

garment was maintained at 60 mmHg and the G-suit was maintained at 180 mmHg by separate regulators adjusted in synchrony with the mean airway pressures.

EPAP (expiratory positive airway pressure) sessions were carried out using a modified aviator mask connected to an EPAP apparatus in series with the expiratory port of the mask. This apparatus consisted of a specialized expiratory hose immersed to a water depth equivalent to 70 mmHg in a specialized closed water bath that allowed for expired gas collection. PPB pressure was maintained at 50 mmHg via the COMBAT EDGE manside test station regulator such that overall mean airway pressures were held at 60 mmHg (Figure 3). Chest counterpressure and G-suit pressure were maintained at 60 and 180 mmHg as above.

High frequency oscillatory tests (Osc) at mean mouthpiece pressures up to 60 mmHg were performed by adapting a Bird VDR 4 Percussionator to fit a special port on a modified aviator mask. Baseline PPB was provided with the standard COMBAT EDGE apparatus while Percussionator frequencies of 6 Hz (9 subjects) or 12 Hz (2 subjects) were added. Mean airway pressures were maintained at 60 mmHg with peak to peak pressure swings ranging from 55 to 65 mmHg. Chest counterpressure and G-suit pressure were maintained at 60 and 180 mmHg respectively with independent regulators that were adjusted in conjunction with the increase in mean airway pressure.

Exhaled gas from the oronasal mask during standard PPB and oscillatory measurements and from the EPAP apparatus was directed through a #4 Fleisch pneumotachograph connected to a Validyne CD-19A carrier demodulator, MP 45-30 transducer, and FV-156 flow integrator for on-line ventilatory measurements. Volume calibration was achieved prior to each experiment using a standard 3 liter calibration syringe (Warren E Collins, Braintree, MA). Volumetric determination during pressure support experiments was recorded directly from analog outputs on the Bear 1000 ventilator.

For all experiments exhaled gas was conducted through standard 38 mm ID corrugated respiratory tubing into 60L Douglas bags for subsequent volume determination. Douglas bag volume was measured using a calibrated model DTM-325-4 dry gasometer (American Meter Company, Nebraska City, NE).

*Cardiovascular Monitoring:* Model T12AD-R disposable pressure transducers (Viggo-Spectramed, Oxnard, CA) for the mask ( $P_m$ ), arterial pressures ( $P_{art}$ ), and at altitude for the central venous (CVP) and pulmonary artery ( $P_{pa}$ ) pressures were connected either directly (surface) or via through-hull penetrators to Space Lab model 512 and 514 patient monitors (Space Labs, Hillsboro, OR). A 5-lead EKG was similarly connected to the Space Labs model 512. Pressure transducers were calibrated with an aneroid gauge prior to each experimental run and referenced to a point 5 cm below the sternal notch with the subject sitting in the experimental position.

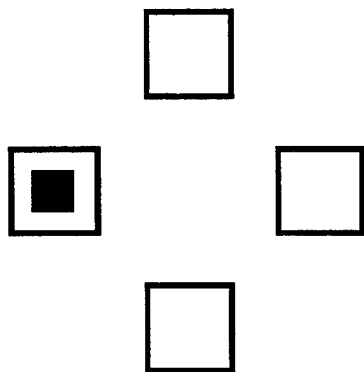
*Measurement of End Expiratory and Arterial Carbon Dioxide Tension:* End expiratory  $CO_2$  tension ( $P_{ET}CO_2$ ) was measured both at the surface and at altitude with a

Novamatrix Capnogard model 1250 CO<sub>2</sub> analyzer. Sample rates were measured to be 150 ml per minute.

*Cognitive Testing:* Subjects were administered a modified version of the Tri-Service Cognitive Battery (UTC-PAB/AGARD Stress Battery, Naval Aerospace Medical Research Laboratory, Pensacola Florida, Aug 1991) during each experimental condition. The subset of tests chosen were selected on the basis of their tendency to be abnormal during hypoxia. These tests were repeated from 4 to 6 times prior to the day of study until the subjects demonstrated by test results that they had reached a learning plateau for each test. The modified battery consisted of a reaction time test ("follow the arrows") and a mathematical processing test ("addition/subtraction") presented on a Toshiba 410CDT laptop computer with a 12 inch active matrix screen. The following is an abbreviated description of each test as outlined in the manual.

*Reaction Time:* A cluster of four 15mm X 15mm open squares arranged in a cross formation are presented to the subject in the center of the computer screen (see below). A smaller solid red square randomly appears inside one of the larger open squares. The subject is required to indicate which of the four squares presented on the screen contains the small solid square by pressing the appropriate arrow key on the keypad as quickly as possible. The square will then jump to a different (or the same box) and the subject must again quickly press the corresponding arrow key. The arrow keys on the keypad are arranged in the same spatial orientation as the presented squares: i.e. at the four points of a cross. Subjects are free to choose which hand to use during the practice runs.

### **"Follow the Arrow" reaction time test screen.**



Each trial has the following structure: stimulus presented for up to 5 seconds after which a "failure to respond" score is noted followed by the random appearance of the red square in another target box. Raw data includes response code, reaction time (positive for correct response, negative for incorrect response, zero for no response), interstimulus interval for time uncertainty block. Summary statistics include mean reaction time (RT) for correct responses, standard deviation of RT, number of trials, percentage errors (excluding response failures) percentage of response failures.



**Mathematical Processing:** In this task two digits are presented in the center of the computer screen to the subject, separated by a plus or minus sign. The object is to add or subtract the digits quickly and accurately and then enter the *last single digit* of the answer. Thus  $9 + 8$  would require the subject to add 9 and 8 and then enter 7 for 17. While  $7 - 4$  would require the subject to subtract 4 from 7 and then enter 3.

If the subtraction yields a *negative* number then the subject must automatically add 10 to it and enter the single positive digit that remains. Thus  $3 - 9$  would require the subject to subtract 9 from 3 to get -6 and then add 10 to get the answer 4. Answers are entered onto a standard computer number pad using the subjects preferred hand. Raw data includes composition of the problem, correct response, subject response, error identification and reaction time. Statistics include RT, SD of RT, mean and SD of correct and incorrect responses, number of problems completed, percent errors for addition and subtraction problems, response failures.

**Data Acquisition and Storage:** All signals were digitized to a Macintosh IIfx personal computer (Apple Computers, Cupertino, CA) at 200 Hz using a MacLab Mk III eight-channel data acquisition system (Analog Digital Instruments, Milford, MA). Data were transferred to an Excel spreadsheet (Microsoft, Redmond, WA) for subsequent statistical analysis.

### **Subject Instrumentation**

On the morning of the study the flight helmet, face mask, chest counterpressure vest and anti-G suit were fitted to the subject prior to any medical intervention. The subject's skin was prepared for EKG electrode placement with Omniprep (DO Weaver and Company, Aurora, CO). Silvon Diaphoretic EKG electrodes (ND, Dayton, OH) were applied. Prior to insertion of the arterial catheter, adequacy of ulnar collateral circulation was established in all subjects using the Allen Test. Using local anesthesia, a 20 gauge, 2 inch arterial catheter was placed in the radial artery of the non-dominant wrist.

An 8.5 French rapid infusion introducer with a side port hemostasis valve (Arrow, Reading, PA) was inserted into the basilic vein prior to the altitude experiments. A #7 French Edwards Swan-Ganz TD pulmonary artery catheter (Baxter, Irvine, CA) was inserted into the main pulmonary artery under radiographic imaging and continuous EKG and pressure monitoring. This catheter has central venous and pulmonary artery pressure/sampling ports, a balloon tip for pulmonary capillary wedge pressure determination and thermistors for thermodilution cardiac output determination.

## Cardiopulmonary Measurements

Subjects were continuously monitored by a physician for fatigue, mental status changes, electrocardiographic changes and blood pressures. Digitized data were collected during the ten minutes before and after each study and later analyzed for heart rate, systolic, diastolic and mean arterial blood pressures, mean pulmonary artery and CVP pressures, mean mask pressures, respiratory rate, tidal volume. Cardiopulmonary measurements were taken over a 10-20 second period following the administration of the neurocognitive test battery. All pressures were referenced to a point 5 cm below the sternal notch with the subject in the resting position.

*Minute ventilation:* During runs at increased mask pressure, when intrathoracic pressure exceeded ambient pressure and additional gas was injected into the circuit (e.g. by the oscillator), it was observed that the volume of gas collected in the Douglas bags significantly exceeded true minute ventilation, which was therefore not reported. This phenomenon does not affect blood gas measurements.

## Statistics

In order to test the effect of experimental conditions, a factorial ANOVA was used. Statistical significance was defined as  $P < 0.05$ . When statistically significant effects were observed, post-hoc paired comparisons were made using the Bonferroni-Dunn method. Statistical calculations were performed on an IBM compatible personal computer using Statview for Windows version 4.5 (Abacus Concepts Inc., Berkeley, CA).

## Safety Considerations

All subjects were healthy volunteers and safety was a prime concern. To minimize potential complications of central venous pressure monitoring and pulmonary artery catheter insertion, advancement of the catheter was performed under fluoroscopy and direct visualization with simultaneous monitoring of arterial pressure and EKG.

During all experimental runs subjects were continuously monitored for EKG, arterial pressure, pulmonary artery and central venous pressures. At least three of the four experimenters were physicians. During chamber exposures an additional physician was outside the chamber monitoring both the physiological signals and a closed circuit video system. All research personnel were in constant communication during chamber exposures with the outside physician and chamber operator.

In order to minimize the risk of decompression sickness and tissue bubble formation, prior to decompression of the altitude chamber all inside personnel and the subject breathed 100% O<sub>2</sub> for at least 60 minutes. Decompression of the chamber from ground level to 24,900 feet simulated altitude was accomplished in 15-16 minutes.

## **Experimental Protocol**

The matrix of experimental conditions is shown in Table 2.

Table 2: Experimental Conditions

CONDITION	PPB <sup>2</sup> (mmHg)	Ventilatory Mode Pressure Support <sup>3</sup> EPAP <sup>4</sup>	Oscillation <sup>5</sup>	Mask	Pressures (mmHg) Chest	G-suit	Insp CO <sub>2</sub> <sup>6</sup>
Ground Level							
Rest Mask <sup>2</sup>	0			0	0	0	
VolHyp <sup>1</sup>	0			0	0	0	
30/0 E	30			30	0	0	
30/0 N	30			30	0	0	●
60/60 E	60			60	60	60	
60/180 E	60			60	60	180	
60/180 N	60			60	60	180	●
60/180 PS	60	●		60	60	180	
60/180 EPAP	60		●	60	60	180	
60/180 LoF E	60			60	60	180	
60/180 HiF E	60		●	60	60	180	
24,900 ft Altitude							
A: Baseline	0			0	0	0	
A: 60/180 E	60			60	60	180	
A: 60/180 N	60			60	60	180	●
A: 60/180 HiF E	60		●	60	60	180	
A: 60/180 HiF N	60		●	60	60	180	●

<sup>1</sup>Voluntary Hyperpnea: Volunteers hyperventilated at a rate they could maintain for 5 minutes.

<sup>2</sup>Aviator mask, COMBAT EDGE in usual configuration

<sup>3</sup>Pressure support ventilation with modified Bear 1000 ventilator

<sup>4</sup>Modified EPAP apparatus connected to expiratory valve of aviator mask

<sup>5</sup>Bird VDR-4 Percussionator

<sup>6</sup>inspired carbon dioxide added to the breathing gas as described in the methods

All subjects underwent the above series of breathing test conditions under normobaric conditions in random sequence with a minimum 15 minute rest period between tests. A new intervention was not started until heart rate, blood pressure and respiratory rate returned to baseline values. Neurocognitive testing was begun once steady state breathing, heart rate and blood pressure was achieved (usually 2-3 minutes). Cardiopulmonary measurements were taken over a 1 minute period following the neurocognitive testing period. Mean mask pressures were maintained at 60 mmHg during all studies. This required adjusting the Bear 1000 pressure support ventilator to provide 50 mmHg inspiratory support with a 70 mmHg expiratory pressure. Oscillations were performed at 6 Hz (9 subjects) and 12 Hz (2 subjects) using the Bird Percussionator modified to function at the 60 mmHg mean PPB (CPAP) pressure supplied through the COMBAT EDGE aviator mask.

During the normocapnic experiments breathing gas was obtained from a series of pre-mixed and analyzed gas cylinders containing either 2 or 4% inspired CO<sub>2</sub>. The particular gas chosen for a given experiment depended on a given subject's degree of hyperventilation and hypocapnia during a previous run. Preliminary studies showed that this range of inspiratory CO<sub>2</sub> was sufficient to allow normalization of arterial CO<sub>2</sub> tensions despite involuntary hyperventilation.

Initially, both 6 and 12 Hz oscillation was incorporated into the protocol. However, a need to reduce the time for which each subject was exposed to PPB (in order to minimize fatigue) precluded the use of both modes in all experiments. During the ground level experiments, 6 Hz was the frequency used. It became apparent (see below) that oscillation at this frequency did not inhibit hyperventilation. However, in one of two subjects in whom 12 Hz oscillation was also administered, PCO<sub>2</sub> at the higher frequency was normal. Therefore, 12 Hz was used for the altitude studies.

## RESULTS

**Complications:** Facial and neck petechiae were frequently observed after PPB. One subject (DH) demonstrated such widespread distribution following 60 mmHg PPB that altitude, EPAP and oscillatory measurements were not attempted.

All subjects had difficulty maintaining consistent levels of ventilation without mask leaks or respiratory muscle fatigue while breathing with the EPAP apparatus. Due to the inconsistency in ventilation and the obvious adverse cardiopulmonary effects of this ventilatory mode it was decided to eliminate it from the experimental protocol for the last three volunteers.

One subject (MB) was able to sustain ventilation for only 3 to 5 minutes during 60/60 PPB, PS, and oscillation secondary to gastrointestinal discomfort caused by aerophagia.

On-line calculation of minute ventilation was complicated during inspiratory pressure support and oscillatory measurements by the inability to quantify the amount of gas injected into the breathing circuit by the external ventilators. During PPB there were occasions where a free flow of gas across the breathing mask made accurate determination of minute ventilation difficult. Ventilatory measurements during EPAP studies were complicated by inconsistent mask seal and leakage. Respiratory rate however, was reliably measured under all conditions from both mouthpiece pressure swings as well as integrated flow signals. Degree of hyperventilation was assessed by level of hypocapnia achieved during each run.

End-tidal PCO<sub>2</sub> values could not be consistently collected, as the capnographs would not function reliably at 24,900 ft.

Two to three subjects in each eucapnia experiment complained of tingling extremities at the end of each study. One subject (GH) complained of tingling, tremor and tetany in the fingers following the eucapneic oscillatory run at altitude and the 30/0 eucapnia run at ground level. TW complained of tremor following the 60/180 PPB ground level run. BA complained of "feeling hot" during the normocapneic 30/0 PPB at ground level while inspiring 4% carbon dioxide.

One subject (GH) experienced a transient loss of consciousness immediately following the performance of the 60/180 eucapneic PPB at altitude. This appeared to be related to a deflation of the G-suit prior to reduction in mask and chest counterpressure and consequent cardiovascular collapse.

**Experimental Results:** Raw data are shown in the tables on pages 17-25 and the graphs on pages 26-33. Statistical results are shown on pages 34-56.

PaCO<sub>2</sub>

Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA	44.3	31.4	19.0	18.5	40.0	15.1	18.3	43.3	16.0	18.7	14.2	
DH	35.2	34.9	22.4	33.6		36.3	37.7		24.4			
FC		45.1		25.4			27.8		20.7	25.7	28.0	
GH	44.0	31.8	16.4	11.6	22.2	11.8	14.9	20.8	12.0	16.2	9.3	
MB	38.5	38.3	17.3	29.1	44.0	19.5	20.6	42.7	14.9			40.6
MH	41.2	39.7	21.5	21.3	27.7	22.8	21.4	35.9	18.4	37.3	23.7	
NH	40.0	32.2	23.7	18.4	29.9	20.0	18.7	30.7	17.4	22.3	19.8	
RB	46.1	46.0	23.4	51.5	45.6	42.1	48.0	49.4	22.6	35.6	41.2	
SA	38.7	41.1	17.5	22.0	38.9	19.0	19.1	40.6			22.1	20.1
TW	42.7	29.8	17.5	20.5	28.6	22.5	24.3	32.7	21.5	22.8	21.2	
Mean	41.2	37.0	19.9	25.2	34.6	23.2	25.1	37.0	18.7	25.5	23.2	30.4
SD	3.44	5.87	2.89	11.06	8.59	9.79	10.29	8.95	4.00	8.08	9.22	14.50
CI	2.25	3.64	1.89	6.86	5.95	6.40	6.38	6.20	2.61	5.98	6.03	20.09

Heart rate

Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA		65.9	61.8	85.9	62.2	110.4	84.3	75.8	97.6	91.5	121.3	
DH		63.7	85.3	69.9		67.9	69.4		68.2			
FC		68.0		87.7								
GH		90.0	100.6	137.0	120.0	160.2	142.0	121.0	151.0	70.6	75.0	74.5
MB		63.7	85.6	87.9	98.4	122.0	108.1	80.2	108.1			
MH		60.8	67.2	76.6	61.4	69.9	70.0	64.9	71.3	67.5	64.5	
NH		73.7	79.6	89.0	95.2	104.7	98.2	87.0	99.1	107.3	88.6	
RB		56.5	64.6	62.6	71.6	81.0	71.4	59.8	69.7	63.5	68.6	
SA		66.2	84.2	83.3	80.8	92.5	70.8	60.6			69.0	80.5
TW		49.5	62.8	77.1	69.5	81.4	61.4	54.6	65.4	71.1	74.2	
Mean		65.8	76.9	85.7	82.4	98.9	86.2	75.5	91.3	78.6	80.2	77.5
SD		10.74	13.42	19.99	20.59	29.43	25.88	21.52	29.32	17.10	19.70	4.24
CI		6.66	8.77	12.39	14.27	19.22	16.91	14.91	20.32	13.68	14.60	5.88

PaCO <sub>2</sub>	Subject	Altitude Baseline	60/180 E		60/180 N		60/180 Hi F E		60/180 Hi F N		GL Post	
			Alt		Alt		Alt		Alt		Alt	
	BA	42.1	19.6	39.8	39.8	18.1	39.8	38.5				
	DH											
	FC											
	GH	42.2	13.1	37.8	40.1	12.7	40.1	31.8				
	MB	none	28.8	40.0	41.4	32.5	41.4	32.8				
	MH											
	NH	36.0	26.6	41.6	41.5	32.3	41.5	37.6				
	RB											
	SA											
	TW											
	Mean	40.1	22.0	39.8	40.7	23.9	40.7	35.2				
	SD	3.55	7.13	1.56	0.88	10.06	0.88	3.36				
	CI	4.02	6.98	1.53	0.86	9.86	0.86	3.30				
Heart rate	Subject	Altitude Baseline	60/180 E		60/180 N		60/180 Hi F E		60/180 Hi F N		GL Post	
	BA		83.6	72.1	80.7	81.7						
	DH											
	FC											
	GH		140.2	124.0	106.0	131.0						
	MB		81.2	84.5	86.2	81.3						
	MH											
	NH		79.3	81.7	72.1	79.7						
	RB											
	SA											
	TW											
	Mean		96.1	90.6	86.3	93.4						
	SD		29.47	22.91	14.39	25.06						
	CI		28.88	22.45	14.10	24.56						



Mean Part

Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA		70.4	75.0	92.0	60.5	115.7	134.3	141.0	116.1	128.0	116.3	
DH		82.9	82.0	102.4		132.5	143.0		137.9			
FC		93.0	105.0			147.4			132.1	137.7	139.7	
GH		88.6	93.5	106.5	107.0	121.6	136.0	144.3	128.1	143.8	127.4	
MB		82.9	79.4	97.6	106.6	120.5	143.7	146.8	125.2			
MH		82.6	82.3	103.8	97.1	125.3	137.4	138.2	132.8	143.0	145.0	
NH		80.5	80.6	97.3	94.4	115.9	130.3	130.8	125.9	135.0	126.0	
RB		81.7	90.7	67.9	56.6	111.2	132.5	144.2	130.6	136.8	90.7	
SA		92.9	100.2	109.7	112.7	129.8	146.5	142.4			140.3	
TW		87.3	91.2	102.8	102.2	128.0	141.5	140.6	102.2	141.6	134.5	
Mean		84.3	86.1	98.5	92.1	124.8	138.3	141.0	125.6	138.0	127.5	
SD		6.66	8.13	11.90	21.55	10.44	5.58	4.92	10.71	5.51	17.52	
CI		4.12	5.31	7.37	14.93	6.47	3.65	3.41	7.00	4.08	12.14	

Respiratory Rate

Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA		12.8	26.4	8.5	12.7	21.0	10.7	11.2	21.8	16.9	30.2	
DH		8.6	41.2	8.3		11.2	9.5		21.3			
FC		7.1		5.9								
GH		12.4	26.2	21.6	17.9	28.0	28.9	24.2	23.4	23.6	31.1	
MB		8.6	9.4	14.0	17.2	23.0	30.4	21.3	35.7			
MH		11.1	35.9	16.4	16.3	19.3	21.6	15.2	33.1	12.1	20.3	
NH		7.4	66.6	14.3	15.8	21.9	13.8	15.6	23.3	21.7	23.3	
RB		10.9	35.5	21.6	11.0	17.7	9.1	23.9	38.8	18.5	23.8	
SA		7.7	38.8	7.6	7.5	13.8	11.8	10.2			12.0	
TW		7.8	21.8	10.0	8.2	9.4	9.6	10.0	11.8	11.0	11.7	
Mean		9.4	33.5	12.8	13.3	18.4	16.2	16.5	26.2	17.3	21.8	
SD		2.15	15.87	5.70	4.09	6.00	8.56	5.97	8.97	5.05	7.78	
CI		1.33	10.37	3.53	2.83	3.92	5.59	4.14	6.22	4.04	5.77	

Mean Part	Subject	Altitude Baseline	Mean Part			
			60/180 E	60/180 N	60/180 Hi F E	60/180 Hi F N GL Post
Mean Part	BA		144.8	135.1	140.9	142.9
	DH					
	FC					
	GH		133.4	142.9	132.6	139.4
	MB		140.1	140.5	135.9	137.5
	MH					
	NH		138.7	142.2	135.1	141.3
	RB					
	SA					
	TW					
Respiratory Rate	Mean		139.2	140.2	136.1	140.3
	SD		4.69	3.55	3.48	2.35
	CI		4.60	3.48	3.41	2.30
	Subject	Altitude Baseline	60/180 E	60/180 N	60/180 Hi F E	60/180 Hi F N GL Post
	BA	6.2	20.2	13.4	21.7	12.1
	DH					
	FC					
	GH	10.8	26.7	17.0	21.7	15.2
	MB	29.1	31.1	28.8	38.2	27.8
	MH					
Respiratory Rate	NH	14.0	19.8	17.8	25.7	31.8
	RB					
	SA					
	TW					
	Mean	15.0	24.5	19.3	26.8	21.7
	SD	9.91	5.45	6.65	7.81	9.55
	CI	9.72	5.34	6.51	7.66	9.36

PaO2

Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA	86.0	115.0	127.0	134.0	138.0	147.0	141.0	140.0	147.0	152.0	149.0	
DH	97.0	102.0	128.0	102.0		104.0	104.0		131.0		130.0	
FC		92.0	127.0				133.0		135.0	136.0		
GH	99.0	118.0	138.0	139.0	144.0	141.0	144.0	142.0	143.0	142.0		90.0
MB	87.0	83.0	136.0	114.0	119.0	132.0	136.0	122.0	138.0		118.0	
MH	90.0	91.0	128.0	134.0	134.0	132.0	137.0	135.0	144.0	95.0	139.0	
NH	102.0	114.0	129.0	132.0	127.0	133.0	135.0	132.0	139.0	135.0	139.0	
RB	90.0	90.0	134.0	72.0	102.0	100.0	84.0	104.0	141.0	122.0	83.0	141.0
SA	87.0	81.0	126.0	119.0	137.0	131.0	137.0	145.0			134.0	
TW	89.0	114.0	129.0	127.0	133.0	131.0	131.0	134.0	139.0	135.0	144.0	
Mean	91.9	100.0	130.6	120.0	129.3	127.9	128.2	131.8	139.7	131.0	129.5	115.5
SD	5.88	14.30	4.30	20.17	13.33	15.67	18.99	13.25	4.82	18.24	21.00	36.06
CI	3.84	8.86	2.81	12.50	9.24	10.24	11.77	9.18	3.15	13.51	14.55	49.98

[H+]

Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA	39.8	31.6	23.4	24.5	37.2	21.4	22.9	39.8	20.4	22.9	19.5	
DH	38.3	39.0	29.0	37.8		40.6	40.5		30.7			
FC		38.0		27.5			28.8		24.5	28.2	28.8	
GH	39.8	33.1	21.9	19.1	27.5	20.0	21.9	27.5	20.4	22.9	17.4	40.6
MB	37.6	38.2	23.2	31.8	41.6	25.7	25.5	41.0	21.9		31.3	
MH	37.2	37.2	24.5	24.0	31.6	25.7	28.2	32.4	23.4	35.5	26.9	
NH	38.0	31.6	28.8	24.0	35.5	26.9	24.0	33.1	22.9	27.5	25.1	
RB	40.7	40.7	26.3	44.1	41.7	38.9	42.7	43.7	26.3	35.5	38.0	25.2
SA	38.3	39.3	23.0	26.7	39.6	25.0	24.3	40.0	25.1		26.7	
TW	38.0	31.6	22.4	25.1	30.9	26.9	28.2	33.1	25.1	26.9	25.1	
Mean	38.6	36.0	24.7	28.5	35.7	27.9	28.7	36.3	24.0	28.5	26.6	32.9
SD	1.20	3.62	2.69	7.47	5.27	7.13	7.20	5.54	3.23	5.22	6.10	10.83
CI	0.78	2.25	1.76	4.63	3.65	4.66	4.46	3.84	2.11	3.87	3.99	15.01

PaO <sub>2</sub>	Subject	Altitude Baseline	60/180				GL Post
			E	N	Hi F E	Hi F N	
	BA	172.0	68.0	80.0	70.0	79.0	84.0
	DH						
	FC						
	GH	180.0	81.0	81.0	81.0	81.0	91.0
	MB		61.0	77.0	61.0	79.0	90.0
	MH						
	NH	181.0	58.0	76.0	52.0	73.0	95.0
	RB						
	SA						
	TW						
	Mean	177.7	67.0	78.5	66.0	78.0	90.0
	SD	4.93	10.23	2.38	12.41	3.46	4.55
	CI	5.58	10.03	2.33	12.16	3.39	4.46
[H+]	Subject	Altitude Baseline	60/180				GL Post
			E	N	Hi F E	Hi F N	
	BA	42.0	26.0	40.1	26.4	40.1	39.8
	DH						
	FC						
	GH	41.4	20.5	40.3	21.3	40.7	35.9
	MB		33.7	42.5	36.5	42.7	37.3
	MH						
	NH	37.1	31.3	40.6	36.1	42.2	40.0
	RB						
	SA						
	TW						
	Mean	40.1	27.9	40.9	30.1	41.4	38.3
	SD	2.68	5.89	1.09	7.47	1.20	1.99
	CI	3.04	5.77	1.07	7.32	1.18	1.95

PetCO<sub>2</sub>

Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA		28.2	16.8	17.1	39.2	12.6	16.5	42.8	12.8	15.2	8.7	
DH		40.4	21.9	9.9		32.3	36.9		22.3			
FC		39.1		38.5								
GH		31.9	15.2			9.2	11.1	10.1	14.9	14.9	7.1	
MB		40.4	17.5	39.8		13.7	16.7	43.9	9.1			
MH		37.5	14.7		31.8	18.6	17.0	28.4	11.9	30.8	11.0	
NH		34.5	17.2		32.8	17.6	18.5	9.8	10.6	19.7	10.4	
RB		41.2	16.7	40.1		26.3	32.4	38.5	14.4	25.6	16.7	
SA		46.0	17.0	41.4	37.6	18.2	22.4	47.4	28.7	20.9	13.8	
TW		27.5	15.7			19.8	24.6	32.8			6.9	

Mean		36.7	17.0	29.6	36.0	18.7	21.8	31.7	15.6	21.2	10.6	
SD		6.00	2.08	15.01	3.42	7.06	8.29	14.76	6.62	6.15	3.60	
CI		3.72	1.36	13.15	3.00	4.61	5.42	10.23	4.58	4.92	2.67	

P<sub>im</sub> Mean

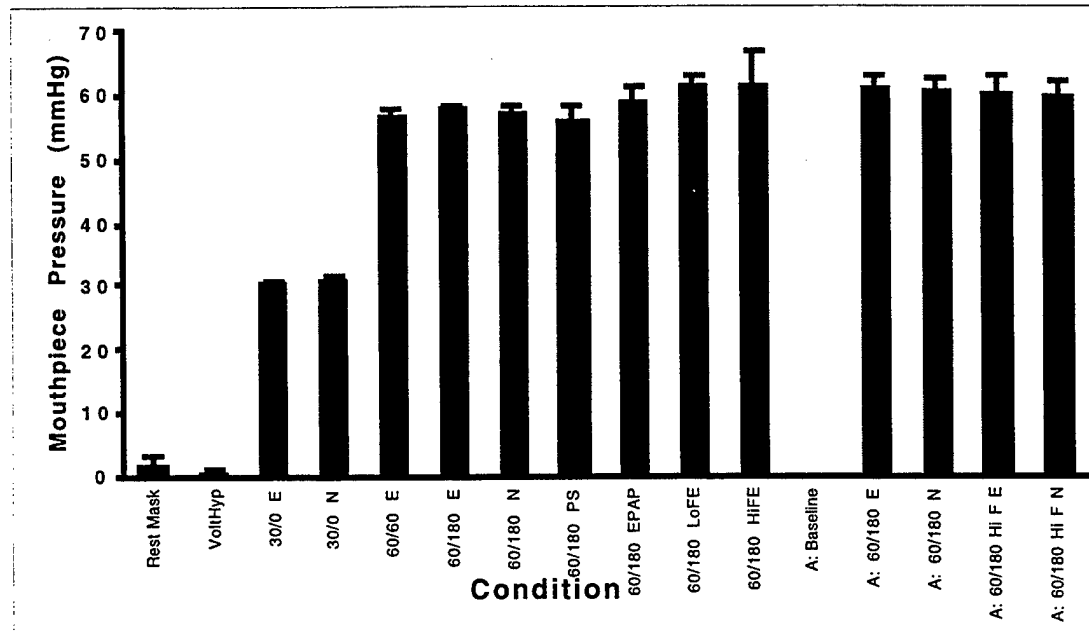
Subject	Rest No Mask	Rest Mask	Volt Hyp	30/0 E	30/0 N	60/60 E	60/180 E	60/180 N	60/180 PS	60/180 EPAP	60/180 LoFE	60/180 HIFE
BA		1.0	-0.4	29.7	31.2	53.8	58.3	57.3	58.4	55.0	58.1	
DH		-1.0	-0.6	29.6		59.0	59.4		55.2			
FC		6.0	0.0	30.2								
GH		4.1	-0.7	29.6	29.8	53.7	56.7	52.5	46.2	57.2	60.3	58.8
MB		-1.0	0.6	30.6	30.1	56.1	57.4	56.7	56.7			
MH		1.4	0.4	31.9	31.7	56.5	56.2	56.4	57.0	60.5	61.7	
NH		4.2	0.7	31.6	32.3	57.7	57.0	60.3	54.6	63.6	61.6	
RB		1.1	1.8	30.3	31.4	58.0	58.7	58.3	58.3	59.8	62.8	
SA		0.2	0.7	30.3	29.7	56.8	57.4	58.1	58.0	56.4	65.1	64.1
TW		0.1	1.4	30.4	31.0	57.9	58.3	56.6	58.0		60.8	

Mean		1.6	0.4	30.4	30.9	56.6	57.7	57.0	55.5	58.7	61.5	61.4
SD		2.38	0.82	0.80	0.95	1.85	1.03	2.24	4.04	3.15	2.17	3.74
CI		1.48	0.51	0.50	0.66	1.21	0.67	1.55	2.80	2.52	1.61	5.18

Pm Mean	Subject	Altitude Baseline	60/180				GL Post
			E	N	Hi F E	Hi F N	
	BA	-1.2	63.3	62.5	62.5	61.6	
	DH						
	FC						
	GH	-0.1	62.4	61.5	61.7	59.6	
	MB	-2.1	58.0	57.4	55.6	56.1	
	MH						
	NH	-0.4	59.6	59.2	60.0	61.0	
	RB						
	SA						
	TW						
	Mean	-1.0	60.8	60.1	59.9	59.6	
	SD	0.91	2.45	2.26	3.06	2.46	
	CI	0.89	2.40	2.22	3.00	2.41	
PvCO2	Subject	Altitude Baseline	60/180				GL Post
			E	N	Hi F E	Hi F N	
	BA	43.2	25.2	44.5	27.5	43.8	44.4
	DH						
	FC						
	GH	48.5	22.6	44.2	22.0	47.9	
	MB		31.7	44.8	38.4	45.4	
	MH						
	NH	41.3	31.3	44.5	37.4	44.6	
	RB						
	SA						
	TW						
	Mean	44.3	27.7	44.5	31.3	45.4	44.4
	SD	3.73	4.52	0.24	7.93	1.77	
	CI	4.22	4.43	0.24	7.77	1.74	

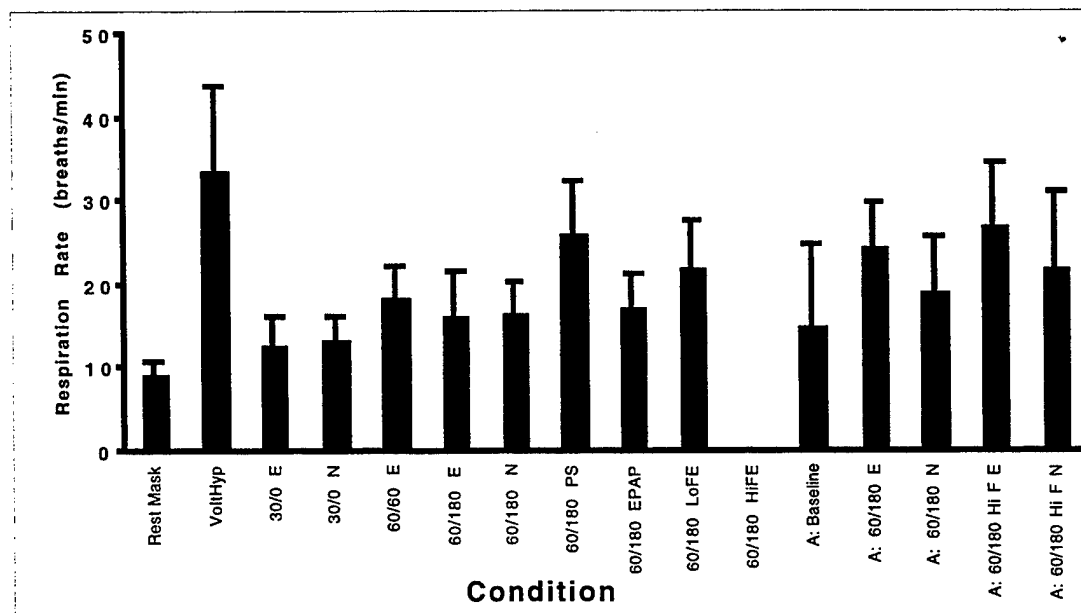
Cardiac Output	Subject	Altitude Baseline	Mean PA Pressure					Altitude Baseline	Subject				
			60/180 E	60/180 N	60/180 Hi F E	60/180 Hi F N	GL Post		60/180 E	60/180 N	60/180 Hi F E	60/180 Hi F N	GL Post
	BA		5.8	5.6	5.5	7.3			65.7	70.6	73.6	63.1	
	DH												
	FC												
	GH		7.5	5.0	6.2	5.4			64.5	64.5	56.7	59.4	
	MB		6.1	6.1	6.5	7.6			62.8	66.5	57.1	60.0	
	MH												
	NH		4.9	5.7	5.3	5.5			66.9	65.8	70.6	62.1	
	RB												
	SA												
	TW												
	Mean		6.1	5.6	5.9	6.4			65.0	66.9	64.5	61.2	
	SD		1.08	0.43	0.55	1.16			1.74	2.62	8.86	1.72	
	CI		1.06	0.42	0.54	1.13			1.71	2.57	8.68	1.69	
SvO2 (IL)													
PvO2	Subject	Altitude Baseline	Mean PA Pressure					Altitude Baseline	Subject				
			60/180 E	60/180 N	60/180 Hi F E	60/180 Hi F N	GL Post		60/180 E	60/180 N	60/180 Hi F E	60/180 Hi F N	GL Post
	BA	44.0	32.0	36.0	32.0	40.0	38.0		75.2	70.7	72.4	76.9	
	DH												
	FC												
	GH	43.0	26.0	30.0	27.0	33.0			65.5	57.9	67.9	63.7	
	MB		33.0	39.0	34.0	41.0			71.6	73.7	70.8	76.8	
	MH												
	NH	45.0	33.0	40.0	33.0	38.0			72.0	75.9	68.3	73.8	
	RB												
	SA												
	TW												
	Mean	44.0	31.0	36.3	31.5	38.0	38.0		71.1	69.6	69.9	72.8	
	SD	1.00	3.37	4.50	3.11	3.56			4.05	8.05	2.13	6.23	
	CI	1.13	3.30	4.41	3.05	3.49			3.97	7.89	2.09	6.11	

### Mean Mask Pressure vs. Experimental Condition



Mean breathing mask pressure was tightly controlled to target levels for all breathing interventions.

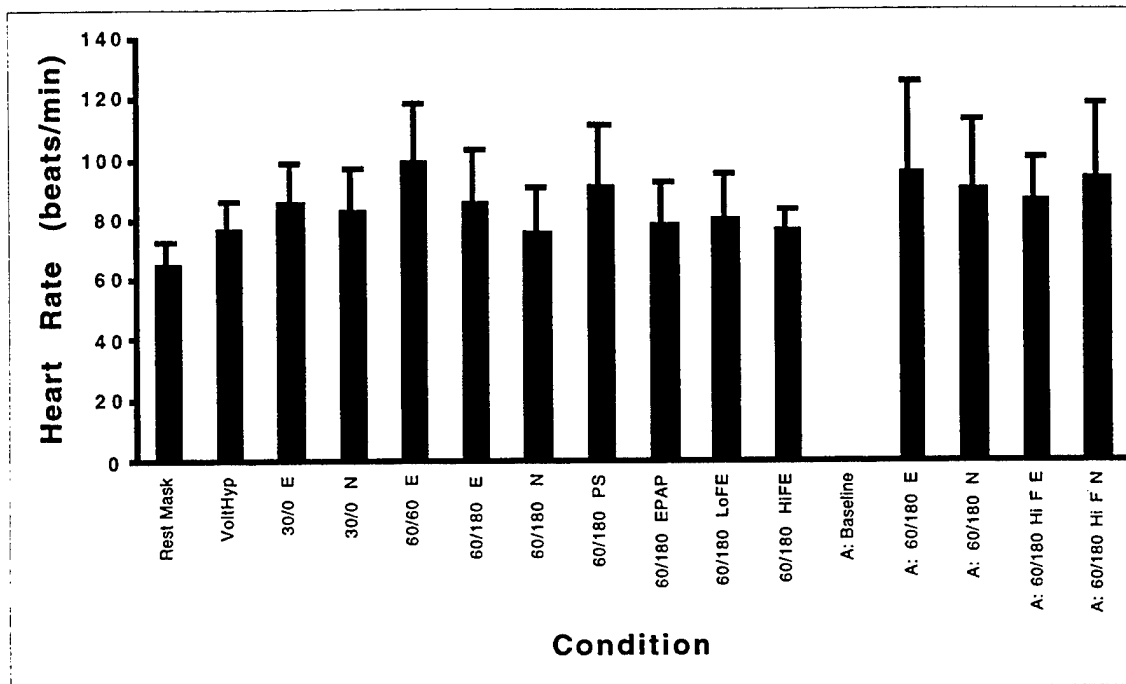
### Respiratory Rate vs. Experimental Condition



Voluntary hyperpnea was achieved primarily by increases in respiratory rate. Breathing frequency also increased during pressure support ventilatory support (PS) when compared to PPB (CPAP). The addition of carbon dioxide to the inspired gas mixture (normocapnia) resulted in lower respiratory rates and improved subjective comfort at altitude. There was little change in respiratory rate in the eucapnia vs. normocapnia experiments at ground level.

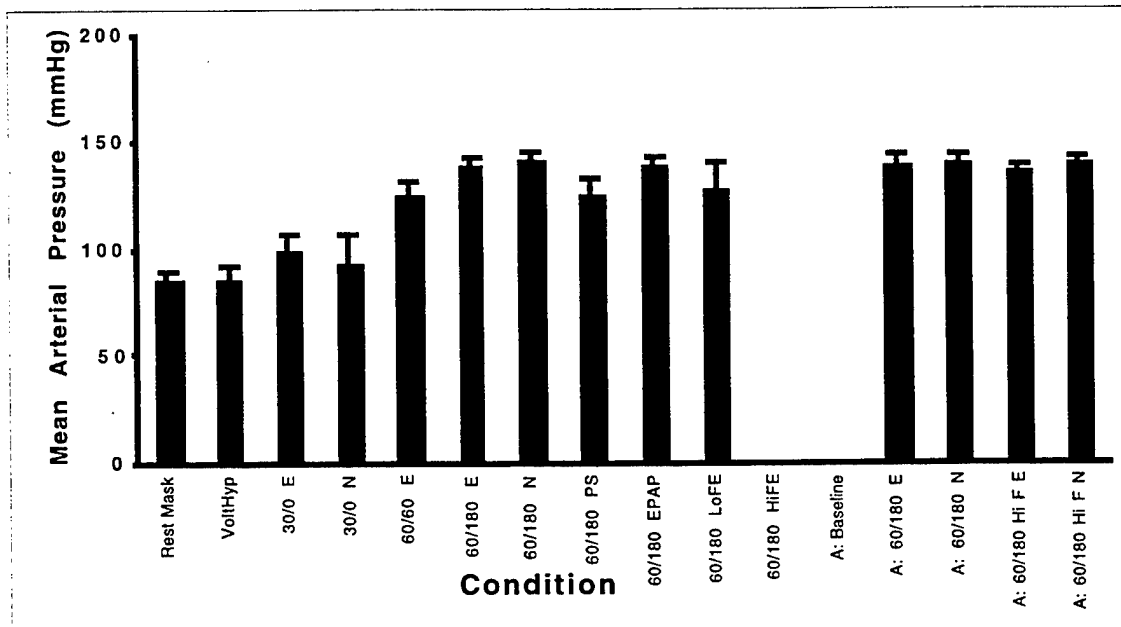


### Heart Rate vs. Experimental Condition



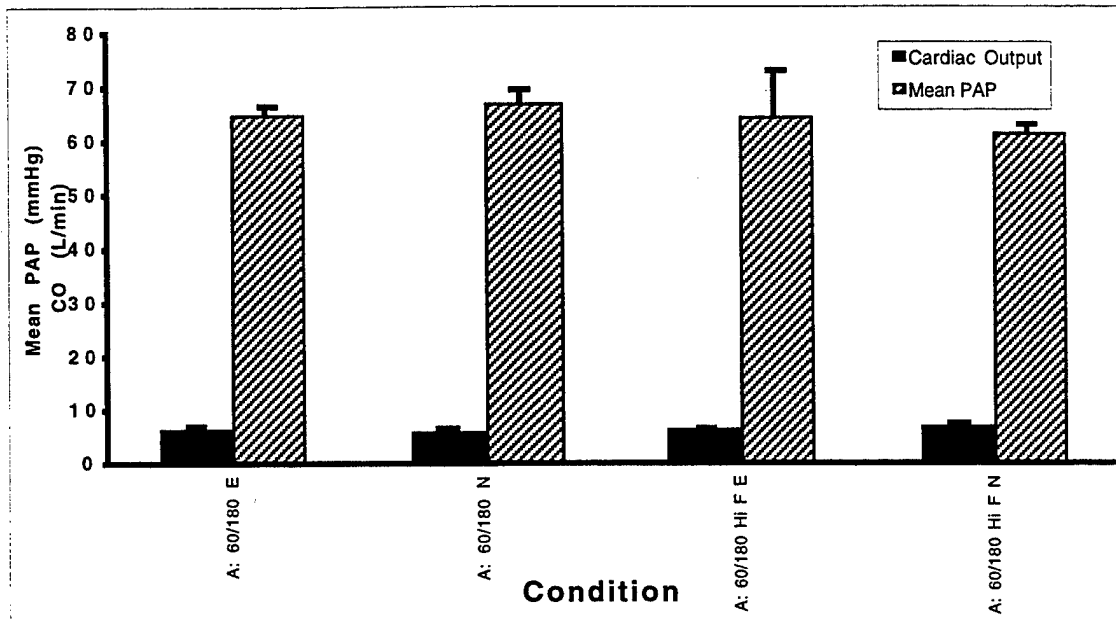
There was no significant effect of any intervention on heart rate.

### Mean Arterial Pressure vs. Experimental Condition



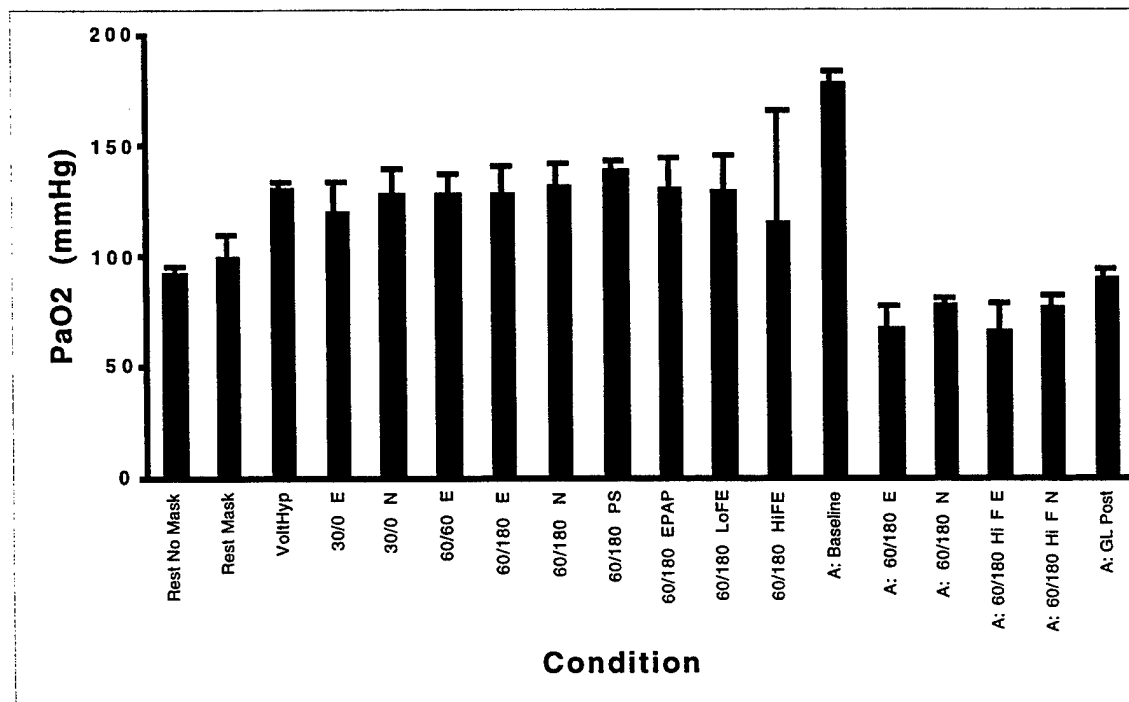
Mean blood pressure increased approximately 10 mmHg over baseline with the addition of 30 mmHg PPB and approximately 45 mmHg over resting values with the addition of 60 mmHg PPB. Phasic PPB did not consistently affect the hemodynamic variables studied. Blood pressure tended to be higher with a 3:1 ratio of G-suit pressure to mean mask pressure (PPB) than with a 1:1 ratio, although the difference was not statistically significant.

### Mean Pulmonary Artery Pressure and Cardiac Output vs. Experimental Condition: Eucapnia and Normocapnia



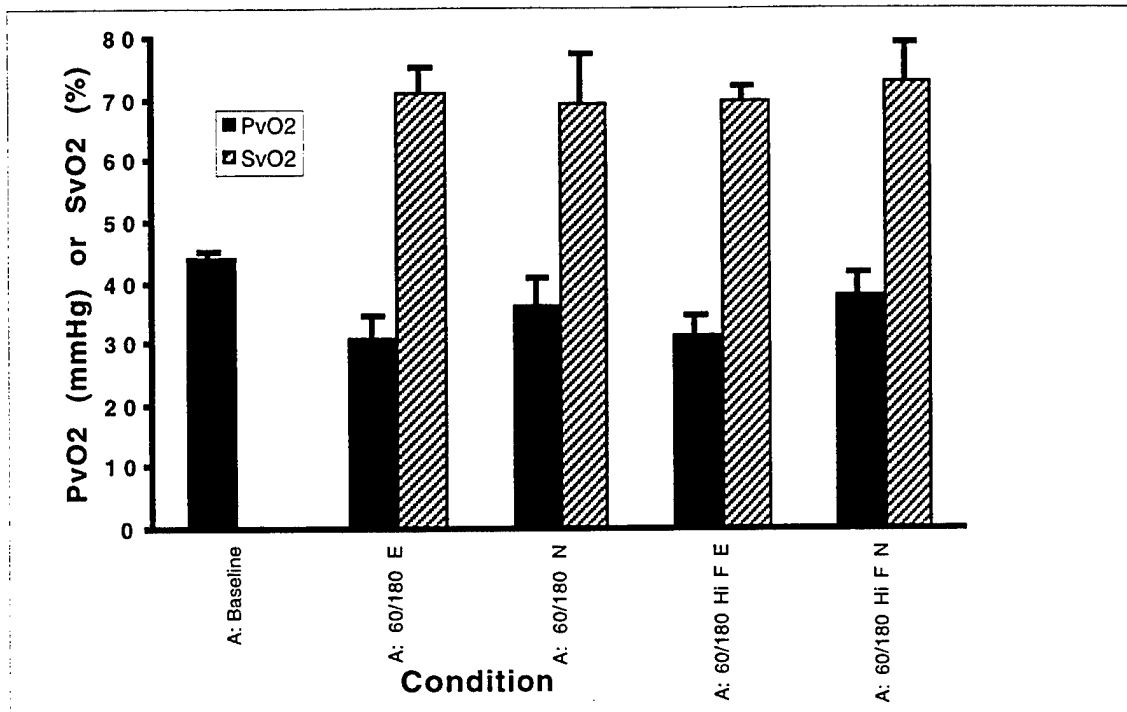
There was no difference in the mean pulmonary artery pressure or cardiac output during PPB or during oscillatory ventilation with or without the addition of carbon dioxide to the breathing gas.

### $P_aO_2$ vs. Experimental Condition



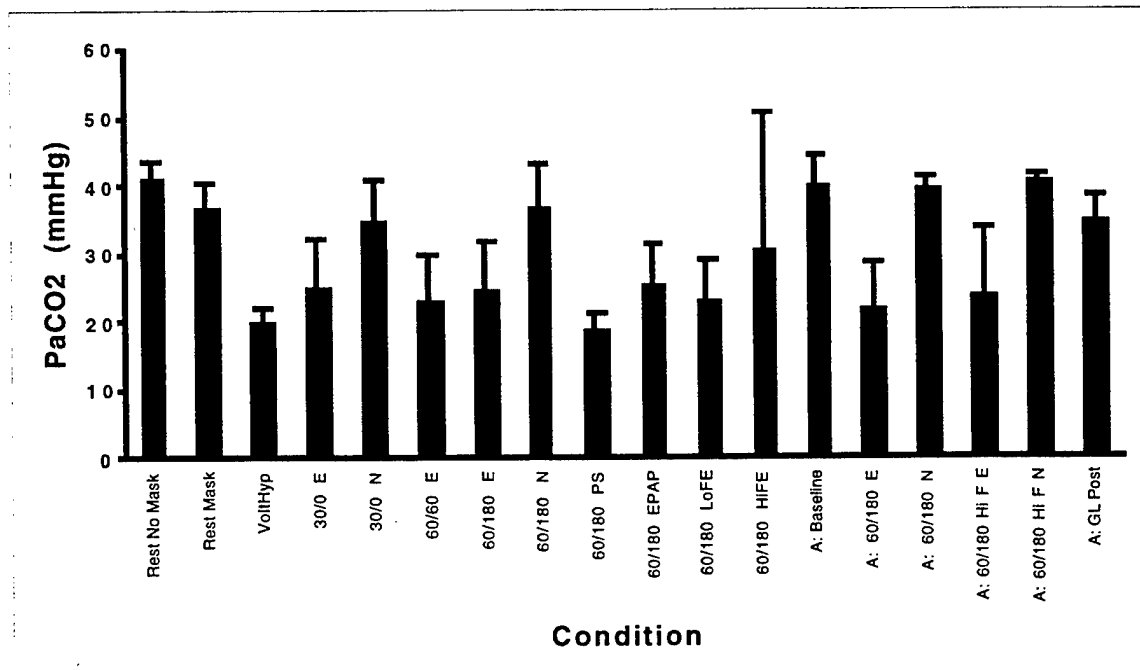
The elevation of  $P_aO_2$  associated with the addition of  $CO_2$  to the inspired gas was not significant at sea level regardless of PPB level but was increasingly so at altitude (30/0E vs. 30/0N and 60/180E vs. 60/180N at surface; 60/180E PPB vs. 60/180N PPB and 60/180E Hi Freq vs. 60/180N Hi Freq. The effect was independent of type of breathing pattern utilized.

### Mixed venous O<sub>2</sub> tension and Hemoglobin Saturation vs. Experimental Condition at 24,900 ft.



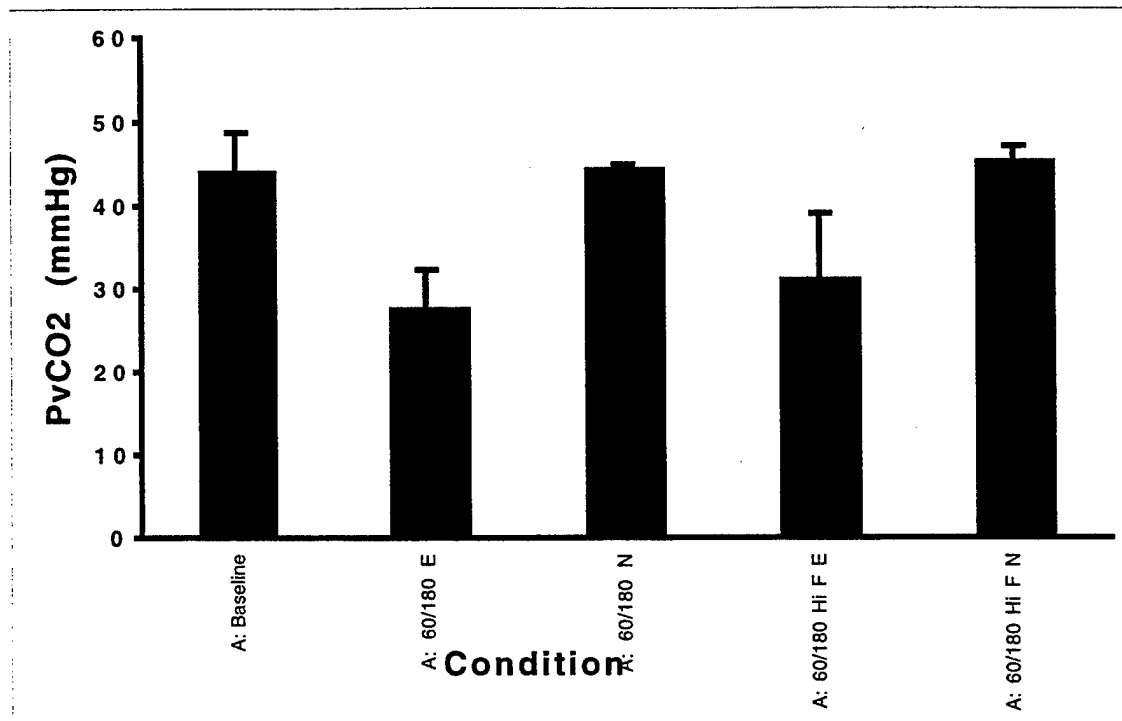
SvO<sub>2</sub> was not significantly altered by Phasic PPB. PvO<sub>2</sub> was lower during 60/180E and 60/180 HiF E (oscillatory ventilation) when compared to baseline.

### PaCO<sub>2</sub> vs. Experimental Condition



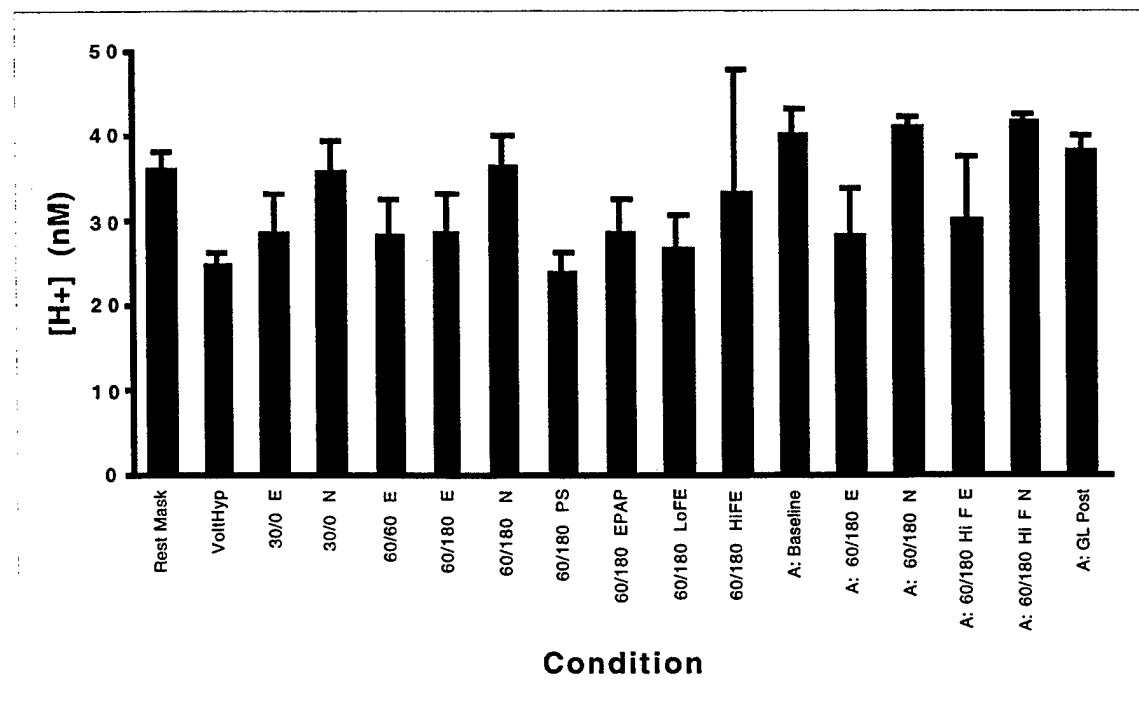
The addition of 4% CO<sub>2</sub> resulted in a mean CO<sub>2</sub> elevation from 24 to 36.9 mmHg. There was no additional benefit of high frequency ventilation in the maintenance of normocapnia with inspired CO<sub>2</sub>.

### $P_vCO_2$ vs. Experimental Condition (altitude)



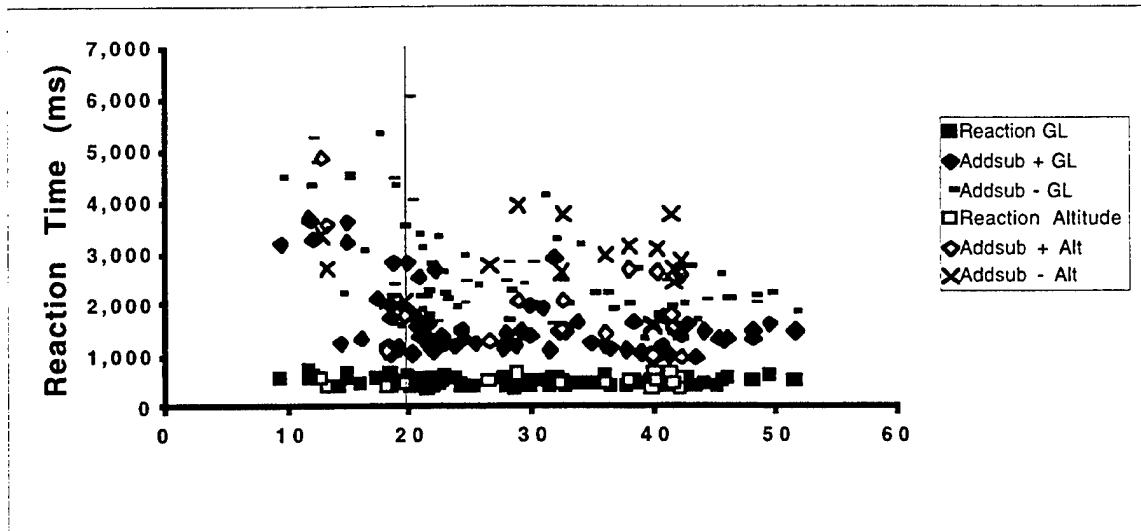
The addition of carbon dioxide to the inspired gas resulted in an increased mixed venous  $CO_2$  tension.

### Arterial Hydrogen Ion Concentration vs. Experimental Condition



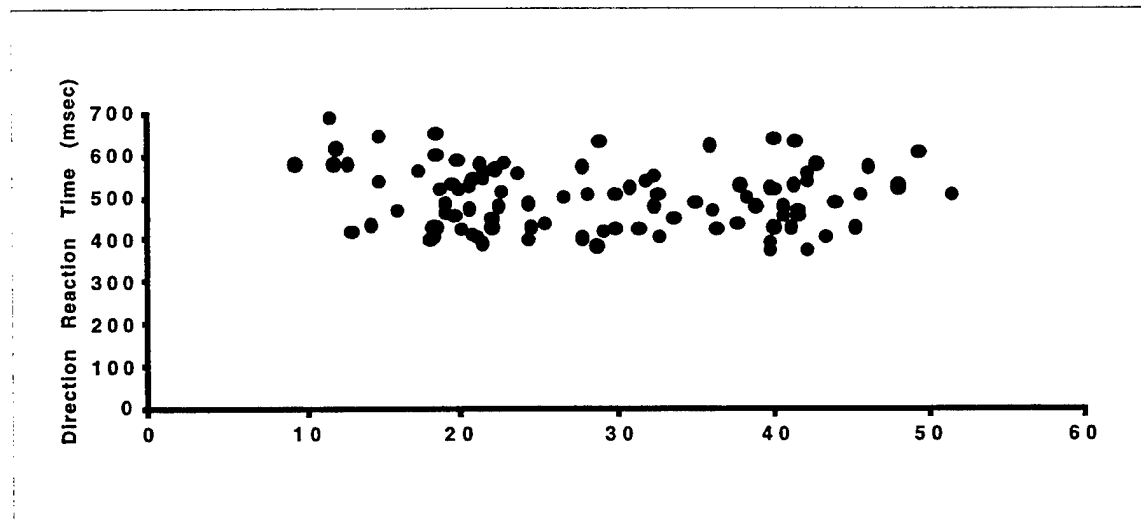
Changes in hydrogen ion concentration followed arterial  $PCO_2$ .

### Reaction Time vs. $P_aCO_2$



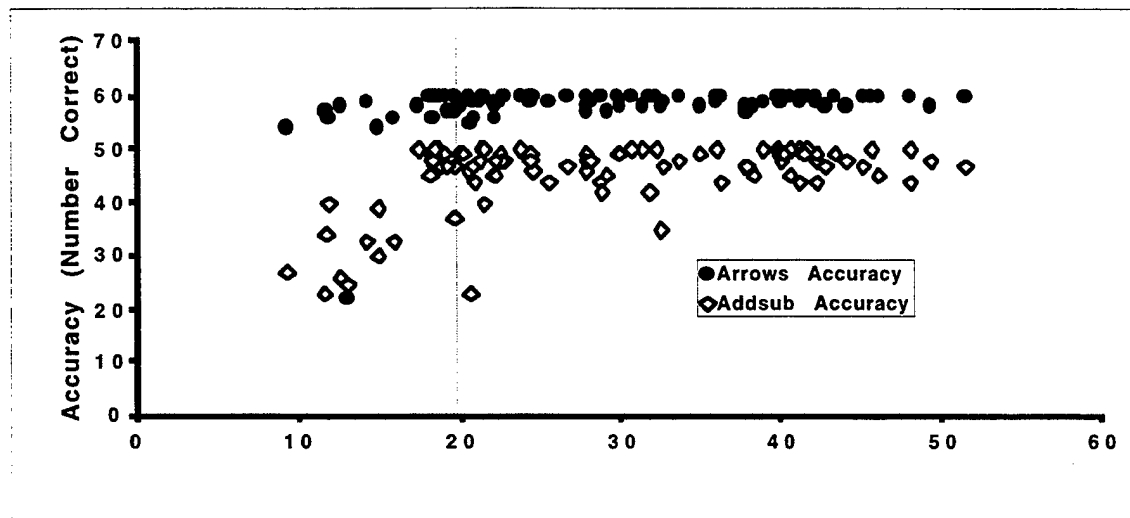
The time to response for the Reaction Time Test ("follow the arrow") was unrelated to either  $P_aCO_2$  or to altitude (open and closed triangles) and was substantially shorter than the reaction time measured during the Mathematical Processing test. Time to response for the Mathematical Processing test (Addsub) was increased at  $P_aCO_2$  below 20mmHg for both addition and subtraction calculations at ground level and at altitude. Reaction time was increased for all subtraction tests when compared to the response time for addition tests and was worse at altitude than at the surface. Reaction time for addition calculations at altitude was faster than that for subtraction at ground level.

### Reaction Time (arrows) vs. $P_aCO_2$



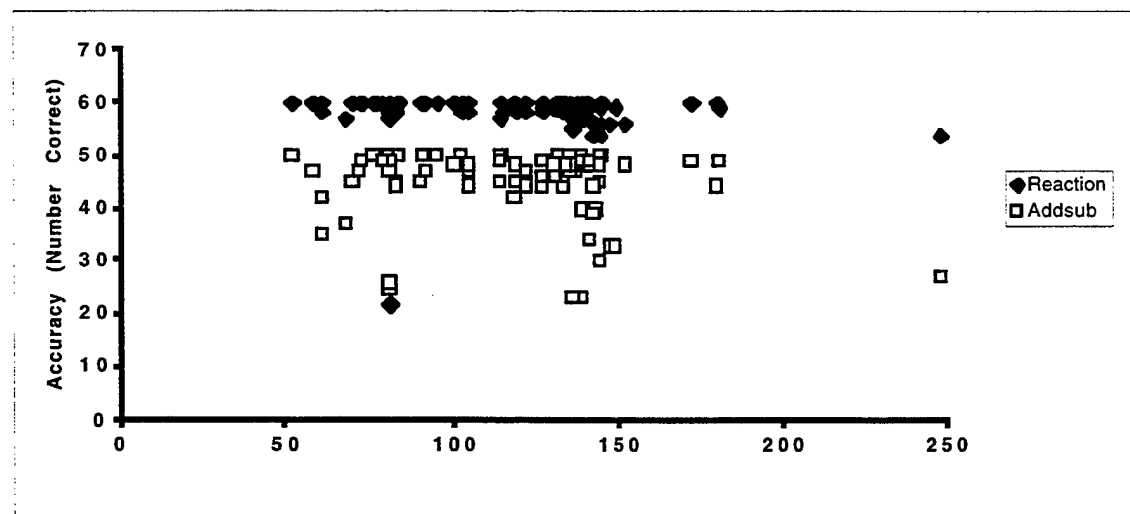
The time to response for the Reaction Time Test ("follow the arrow") was unrelated to either  $P_aCO_2$  or to altitude (altitude and ground level data from previous figure combined).

### Accuracy vs. $P_aCO_2$

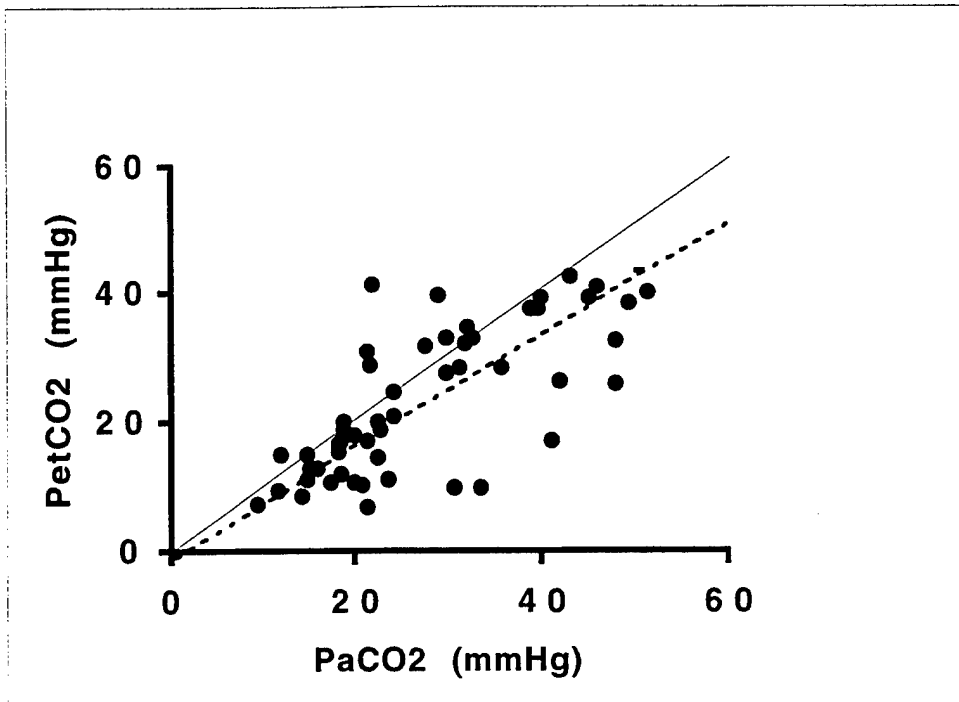


The number of correct responses recorded for all experimental conditions during the Reaction Time test (Arrows, blue symbols) does not correlate with  $P_aCO_2$ . A perfect score is represented by 60 correct responses. Accuracy for the Mathematical Processing (Addsub, red symbols) was consistently lower than for the Reaction Time and unrelated to  $P_aCO_2$  at levels greater than 20mmHg. It was correlated to decreased  $P_aCO_2$  at levels less than 20mmHg. More errors were made during subtraction calculations than during addition.

### Accuracy vs. $P_aO_2$



There was no consistent relationship between accuracy and  $P_aO_2$  for either the Reaction Time test or the Mathematical Processing test.



The relationship between  $P_{et}CO_2$  and  $P_aCO_2$  is shown, along with the line of identity (solid line) and line of least squares best fit (dashed line). There is considerable scatter in the data.  $P_{et}CO_2$  underestimates  $P_aCO_2$  during PPB by up to 25 mmHg.

## ANOVA Table for Heart rate:

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	14	8336.342	595.453	1.261	0.2484
Residual	87	41083.259	472.221		

Model II estimate of between component variance: 18.3

58 cases were omitted due to missing values.

Bonferroni/Dunn for Heart rate:

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value
30/0 E, 30/0 N	3.313	37.836	0.7487
30/0 E, 60/180 E	-0.478	36.65	0.9619
30/0 E, 60/180 EPAP	7.117	41.191	0.5276
30/0 E, 60/180 HiFE	8.2	61.786	0.6274
30/0 E, 60/180 LoFE	5.529	39.309	0.607
30/0 E, 60/180 N	10.213	37.836	0.3246
30/0 E, 60/180 PS	-5.6	37.836	0.5883
30/0 E, 60/60 E	-13.189	36.65	0.19
30/0 E, A: 60/180 E	-10.375	47.19	0.4219
30/0 E, A: 60/180 Hi F E	-0.55	47.19	0.966
30/0 E, A: 60/180 Hi F N	-7.725	47.19	0.5495
30/0 E, A: 60/180 N	-4.875	47.19	0.7055
30/0 E, A: Baseline	85.7		
30/0 E, Rest Mask	19.9	35.672	0.0436
30/0 E, VoltHyp	8.844	36.65	0.3782
30/0 N, 60/180 E	-3.79	38.759	0.7205
30/0 N, 60/180 EPAP	3.804	43.078	0.7466
30/0 N, 60/180 HiFE	4.888	63.06	0.7767
30/0 N, 60/180 LoFE	2.216	41.283	0.8443
30/0 N, 60/180 N	6.9	39.883	0.5271
30/0 N, 60/180 PS	-8.913	39.883	0.4143
30/0 N, 60/60 E	-16.501	38.759	0.1217
30/0 N, A: 60/180 E	-13.688	48.846	0.3065
30/0 N, A: 60/180 Hi F E	-3.862	48.846	0.7723
30/0 N, A: 60/180 Hi F N	-11.037	48.846	0.4091
30/0 N, A: 60/180 N	-8.188	48.846	0.54
30/0 N, A: Baseline	82.388		
30/0 N, Rest Mask	16.588	37.836	0.1112
30/0 N, VoltHyp	5.532	38.759	0.6017
60/180 E, 60/180 EPAP	7.594	42.04	0.509
60/180 E, 60/180 HiFE	8.678	62.355	0.6108
60/180 E, 60/180 LoFE	6.006	40.198	0.5848
60/180 E, 60/180 N	10.69	38.759	0.3141
60/180 E, 60/180 PS	-5.122	38.759	0.6288
60/180 E, 60/60 E	-12.711	37.602	0.218
60/180 E, A: 60/180 E	-9.897	47.933	0.4506
60/180 E, A: 60/180 Hi F E	-0.072	47.933	0.9956
60/180 E, A: 60/180 Hi F N	-7.247	47.933	0.5803
60/180 E, A: 60/180 N	-4.397	47.933	0.7371
60/180 E, A: Baseline	86.178		
60/180 E, Rest Mask	20.378	36.65	0.0443
60/180 E, VoltHyp	9.322	37.602	0.3653
60/180 EPAP, 60/180 HiFE	1.083	65.128	0.9515
60/180 EPAP, 60/180 LoFE	-1.588	44.377	0.8958



60/180 EPAP, 60/180 N	3.096	43.078	0.7926
60/180 EPAP, 60/180 PS	-12.717	43.078	0.2815
60/180 EPAP, 60/60 E	-20.306	42.04	0.0797
60/180 EPAP, A: 60/180 E	-17.492	51.488	0.2157
60/180 EPAP, A: 60/180 Hi F E	-7.667	51.488	0.5861
60/180 EPAP, A: 60/180 Hi F N	-14.842	51.488	0.293
60/180 EPAP, A: 60/180 N	-11.992	51.488	0.395
60/180 EPAP, A: Baseline	78.583	.	.
60/180 EPAP, Rest Mask	12.783	41.191	0.2578
60/180 EPAP, VoltHyp	1.728	42.04	0.8804
60/180 HiFE, 60/180 LoFE	-2.671	63.955	0.8785
60/180 HiFE, 60/180 N	2.013	63.06	0.907
60/180 HiFE, 60/180 PS	-13.8	63.06	0.424
60/180 HiFE, 60/60 E	-21.389	62.355	0.2114
60/180 HiFE, A: 60/180 E	-18.575	69.079	0.3264
60/180 HiFE, A: 60/180 Hi F E	-8.75	69.079	0.6431
60/180 HiFE, A: 60/180 Hi F N	-15.925	69.079	0.3998
60/180 HiFE, A: 60/180 N	-13.075	69.079	0.4891
60/180 HiFE, A: Baseline	77.5	.	.
60/180 HiFE, Rest Mask	11.7	61.786	0.4889
60/180 HiFE, VoltHyp	0.644	62.355	0.9698
60/180 LoFE, 60/180 N	4.684	41.283	0.6781
60/180 LoFE, 60/180 PS	-11.129	41.283	0.3252
60/180 LoFE, 60/60 E	-18.717	40.198	0.091
60/180 LoFE, A: 60/180 E	-15.904	49.996	0.2461
60/180 LoFE, A: 60/180 Hi F E	-6.079	49.996	0.6565
60/180 LoFE, A: 60/180 Hi F N	-13.254	49.996	0.3332
60/180 LoFE, A: 60/180 N	-10.404	49.996	0.447
60/180 LoFE, A: Baseline	80.171	.	.
60/180 LoFE, Rest Mask	14.371	39.309	0.1831
60/180 LoFE, VoltHyp	3.316	40.198	0.7628
60/180 N, 60/180 PS	-15.813	39.883	0.1492
60/180 N, 60/60 E	-23.401	38.759	0.0293
60/180 N, A: 60/180 E	-20.588	48.846	0.1255
60/180 N, A: 60/180 Hi F E	-10.763	48.846	0.4209
60/180 N, A: 60/180 Hi F N	-17.938	48.846	0.1812
60/180 N, A: 60/180 N	-15.088	48.846	0.26
60/180 N, A: Baseline	75.487	.	.
60/180 N, Rest Mask	9.688	37.836	0.3499
60/180 N, VoltHyp	-1.368	38.759	0.8972
60/180 PS, 60/60 E	-7.589	38.759	0.4743
60/180 PS, A: 60/180 E	-4.775	48.846	0.7206
60/180 PS, A: 60/180 Hi F E	5.05	48.846	0.7052
60/180 PS, A: 60/180 Hi F N	-2.125	48.846	0.8735
60/180 PS, A: 60/180 N	0.725	48.846	0.9567
60/180 PS, A: Baseline	91.3	.	.
60/180 PS, Rest Mask	25.5	37.836	0.0153
60/180 PS, VoltHyp	14.444	38.759	0.1749
60/60 E, A: 60/180 E	2.814	47.933	0.8299
60/60 E, A: 60/180 Hi F E	12.639	47.933	0.3358
60/60 E, A: 60/180 Hi F N	5.464	47.933	0.6767
60/60 E, A: 60/180 N	8.314	47.933	0.526
60/60 E, A: Baseline	98.889	.	.
60/60 E, Rest Mask	33.089	36.65	0.0013
60/60 E, VoltHyp	22.033	37.602	0.0343
A: 60/180 E, A: 60/180 Hi F E	9.825	56.403	0.5242
A: 60/180 E, A: 60/180 Hi F N	2.65	56.403	0.8635
A: 60/180 E, A: 60/180 N	5.5	56.403	0.7213
A: 60/180 E, A: Baseline	96.075	.	.

A: 60/180 E, Rest Mask	30.275	47.19	0.0208
A: 60/180 E, VoltHyp	19.219	47.933	0.1447
A: 60/180 Hi F E, A: 60/180 Hi F N	-7.175	56.403	0.6417
A: 60/180 Hi F E, A: 60/180 N	-4.325	56.403	0.779
A: 60/180 Hi F E, A: Baseline	86.25	.	.
A: 60/180 Hi F E, Rest Mask	20.45	47.19	0.1153
A: 60/180 Hi F E, VoltHyp	9.394	47.933	0.4738
A: 60/180 Hi F N, A: 60/180 N	2.85	56.403	0.8533
A: 60/180 Hi F N, A: Baseline	93.425	.	.
A: 60/180 Hi F N, Rest Mask	27.625	47.19	0.0344
A: 60/180 Hi F N, VoltHyp	16.569	47.933	0.2079
A: 60/180 N, A: Baseline	90.575	.	.
A: 60/180 N, Rest Mask	24.775	47.19	0.0572
A: 60/180 N, VoltHyp	13.719	47.933	0.2963
A: Baseline, Rest Mask	-65.8	.	.
A: Baseline, VoltHyp	-76.856	.	.
Rest Mask, VoltHyp	-11.056	36.65	0.2712

Comparisons in this table are not significant unless the corresponding p-value is less than .0004.

58 cases were omitted due to missing values.

## ANOVA Table for Mean Part

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	13	49217.75	3785.981	33.221	<.0001
Residual	90	10256.735	113.964		

Model II estimate of between component variance: 498.05

56 cases were omitted due to missing values.

Bonferroni/Dunn for Mean Part

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value	
30/0 E, 30/0 N	6.356	18.563	0.2126	
30/0 E, 60/180 E	-39.844	17.981	<.0001	S
30/0 E, 60/180 EPAP	-39.485	19.285	<.0001	S
30/0 E, 60/180 HiFE	98.494	.	.	
30/0 E, 60/180 LoFE	-28.994	18.563	<.0001	S
30/0 E, 60/180 N	-42.544	18.563	<.0001	S
30/0 E, 60/180 PS	-27.155	17.981	<.0001	S
30/0 E, 60/60 E	-26.307	17.501	<.0001	S
30/0 E, A: 60/180 E	-40.744	23.152	<.0001	S
30/0 E, A: 60/180 Hi F E	-37.626	23.152	<.0001	S
30/0 E, A: 60/180 Hi F N	-41.779	23.152	<.0001	S
30/0 E, A: 60/180 N	-41.656	23.152	<.0001	S
30/0 E, A: Baseline	98.494	.	.	
30/0 E, Rest Mask	14.216	17.501	0.0037	
30/0 E, VoltHyp	12.401	17.981	0.0132	
30/0 N, 60/180 E	-46.2	19.015	<.0001	S
30/0 N, 60/180 EPAP	-45.841	20.253	<.0001	S
30/0 N, 60/180 HiFE	92.138	.	.	
30/0 N, 60/180 LoFE	-35.35	19.567	<.0001	S
30/0 N, 60/180 N	-48.9	19.567	<.0001	S
30/0 N, 60/180 PS	-33.511	19.015	<.0001	S
30/0 N, 60/60 E	-32.663	18.563	<.0001	S
30/0 N, A: 60/180 E	-47.1	23.964	<.0001	S
30/0 N, A: 60/180 Hi F E	-43.983	23.964	<.0001	S
30/0 N, A: 60/180 Hi F N	-48.135	23.964	<.0001	S
30/0 N, A: 60/180 N	-48.013	23.964	<.0001	S
30/0 N, A: Baseline	92.138	.	.	
30/0 N, Rest Mask	7.86	18.563	0.1241	
30/0 N, VoltHyp	6.044	19.015	0.247	
60/180 E, 60/180 EPAP	0.359	19.721	0.9469	
60/180 E, 60/180 HiFE	138.338	.	.	
60/180 E, 60/180 LoFE	10.85	19.015	0.0393	
60/180 E, 60/180 N	-2.7	19.015	0.604	
60/180 E, 60/180 PS	12.689	18.448	0.0134	
60/180 E, 60/60 E	13.537	17.981	0.007	
60/180 E, A: 60/180 E	-0.9	23.516	0.8888	
60/180 E, A: 60/180 Hi F E	2.218	23.516	0.7304	
60/180 E, A: 60/180 Hi F N	-1.935	23.516	0.7637	
60/180 E, A: 60/180 N	-1.812	23.516	0.7782	
60/180 E, A: Baseline	138.338	.	.	
60/180 E, Rest Mask	54.06	17.981	<.0001	S
60/180 E, VoltHyp	52.244	18.448	<.0001	S
60/180 EPAP, 60/180 HiFE	137.979	.	.	
60/180 EPAP, 60/180 LoFE	10.491	20.253	0.0608	

60/180 EPAP, 60/180 N	-3.059	20.253	0.5812	
60/180 EPAP, 60/180 PS	12.33	19.721	0.0242	
60/180 EPAP, 60/60 E	13.178	19.285	0.0141	
60/180 EPAP, A: 60/180 E	-1.259	24.528	0.8512	
60/180 EPAP, A: 60/180 Hi F E	1.859	24.528	0.7818	
60/180 EPAP, A: 60/180 Hi F N	-2.294	24.528	0.7325	
60/180 EPAP, A: 60/180 N	-2.171	24.528	0.7463	
60/180 EPAP, A: Baseline	137.979	.	.	
60/180 EPAP, Rest Mask	53.701	19.285	<.0001	S
60/180 EPAP, VoltHyp	51.885	19.721	<.0001	S
60/180 HiFE, 60/180 LoFE	-127.488	.	.	
60/180 HiFE, 60/180 N	-141.038	.	.	
60/180 HiFE, 60/180 PS	-125.649	.	.	
60/180 HiFE, 60/60 E	-124.801	.	.	
60/180 HiFE, A: 60/180 E	-139.238	.	.	
60/180 HiFE, A: 60/180 Hi F E	-136.12	.	.	
60/180 HiFE, A: 60/180 Hi F N	-140.273	.	.	
60/180 HiFE, A: 60/180 N	-140.15	.	.	
60/180 HiFE, A: Baseline	0	.	.	
60/180 HiFE, Rest Mask	-84.278	.	.	
60/180 HiFE, VoltHyp	-86.093	.	.	
60/180 LoFE, 60/180 N	-13.55	19.567	0.0128	
60/180 LoFE, 60/180 PS	1.839	19.015	0.7238	
60/180 LoFE, 60/60 E	2.687	18.563	0.597	
60/180 LoFE, A: 60/180 E	-11.75	23.964	0.0756	
60/180 LoFE, A: 60/180 Hi F E	-8.632	23.964	0.19	
60/180 LoFE, A: 60/180 Hi F N	-12.785	23.964	0.0536	
60/180 LoFE, A: 60/180 N	-12.663	23.964	0.0559	
60/180 LoFE, A: Baseline	127.488	.	.	
60/180 LoFE, Rest Mask	43.21	18.563	<.0001	S
60/180 LoFE, VoltHyp	41.394	19.015	<.0001	S
60/180 N, 60/180 PS	15.389	19.015	0.0039	
60/180 N, 60/60 E	16.237	18.563	0.0019	
60/180 N, A: 60/180 E	1.8	23.964	0.7837	
60/180 N, A: 60/180 Hi F E	4.918	23.964	0.4539	
60/180 N, A: 60/180 Hi F N	0.765	23.964	0.9071	
60/180 N, A: 60/180 N	0.887	23.964	0.8923	
60/180 N, A: Baseline	141.038	.	.	
60/180 N, Rest Mask	56.76	18.563	<.0001	S
60/180 N, VoltHyp	54.944	19.015	<.0001	S
60/180 PS, 60/60 E	0.848	17.981	0.8631	
60/180 PS, A: 60/180 E	-13.589	23.516	0.0369	
60/180 PS, A: 60/180 Hi F E	-10.471	23.516	0.1061	
60/180 PS, A: 60/180 Hi F N	-14.624	23.516	0.025	
60/180 PS, A: 60/180 N	-14.501	23.516	0.0262	
60/180 PS, A: Baseline	125.649	.	.	
60/180 PS, Rest Mask	41.371	17.981	<.0001	S
60/180 PS, VoltHyp	39.556	18.448	<.0001	S
60/60 E, A: 60/180 E	-14.437	23.152	0.0246	
60/60 E, A: 60/180 Hi F E	-11.319	23.152	0.0765	
60/60 E, A: 60/180 Hi F N	-15.472	23.152	0.0162	
60/60 E, A: 60/180 N	-15.349	23.152	0.0171	
60/60 E, A: Baseline	124.801	.	.	
60/60 E, Rest Mask	40.523	17.501	<.0001	S
60/60 E, VoltHyp	38.708	17.981	<.0001	S
A: 60/180 E, A: 60/180 Hi F E	3.118	27.672	0.6806	
A: 60/180 E, A: 60/180 Hi F N	-1.035	27.672	0.8912	
A: 60/180 E, A: 60/180 N	-0.913	27.672	0.9041	
A: 60/180 E, A: Baseline	139.238	.	.	

A: 60/180 E, Rest Mask	54.96	23.152	<.0001	S
A: 60/180 E, VoltHyp	53.144	23.516	<.0001	S
A: 60/180 Hi F E, A: 60/180 Hi F N	-4.153	27.672	0.5836	
A: 60/180 Hi F E, A: 60/180 N	-4.03	27.672	0.5947	
A: 60/180 Hi F E, A: Baseline	136.12	.	.	
A: 60/180 Hi F E, Rest Mask	51.842	23.152	<.0001	S
A: 60/180 Hi F E, VoltHyp	50.027	23.516	<.0001	S
A: 60/180 Hi F N, A: 60/180 N	0.122	27.672	0.9871	
A: 60/180 Hi F N, A: Baseline	140.273	.	.	
A: 60/180 Hi F N, Rest Mask	55.995	23.152	<.0001	S
A: 60/180 Hi F N, VoltHyp	54.179	23.516	<.0001	S
A: 60/180 N, A: Baseline	140.15	.	.	
A: 60/180 N, Rest Mask	55.872	23.152	<.0001	S
A: 60/180 N, VoltHyp	54.057	23.516	<.0001	S
A: Baseline, Rest Mask	-84.278	.	.	
A: Baseline, VoltHyp	-86.093	.	.	
Rest Mask, VoltHyp	-1.815	17.981	0.7122	

Comparisons in this table are not significant unless the corresponding p-value is less than .0004.

56 cases were omitted due to missing values.

## ANOVA Table for Respiratory Rate

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	14	4519.239	322.803	5.115	<.0001
Residual	89	5616.854	63.111		

Model II estimate of between component variance: 37.751

56 cases were omitted due to missing values.

Bonferroni/Dunn for Respiratory Rate

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value	
30/0 E, 30/0 N	-0.505	13.82	0.8937	
30/0 E, 60/180 E	-3.336	13.386	0.3633	
30/0 E, 60/180 EPAP	-4.48	15.045	0.2778	
30/0 E, 60/180 HiFE	12.82			
30/0 E, 60/180 LoFE	-8.951	14.358	0.0246	
30/0 E, 60/180 N	-3.63	13.82	0.338	
30/0 E, 60/180 PS	-13.33	13.82	0.0006	
30/0 E, 60/60 E	-5.547	13.386	0.1322	
30/0 E, A: 60/180 E	-11.63	17.236	0.0152	
30/0 E, A: 60/180 Hi F E	-14.005	17.236	0.0037	
30/0 E, A: 60/180 Hi F N	-8.905	17.236	0.0614	
30/0 E, A: 60/180 N	-6.43	17.236	0.1747	
30/0 E, A: Baseline	-2.205	17.236	0.6401	
30/0 E, Rest Mask	3.38	13.029	0.344	
30/0 E, VoltHyp	-20.713	13.386	<.0001	S
30/0 N, 60/180 E	-2.831	14.157	0.4653	
30/0 N, 60/180 EPAP	-3.975	15.734	0.3567	
30/0 N, 60/180 HiFE	13.325			
30/0 N, 60/180 LoFE	-8.446	15.078	0.0429	
30/0 N, 60/180 N	-3.125	14.567	0.4335	
30/0 N, 60/180 PS	-12.825	14.567	0.0017	
30/0 N, 60/60 E	-5.042	14.157	0.1949	
30/0 N, A: 60/180 E	-11.125	17.841	0.0246	
30/0 N, A: 60/180 Hi F E	-13.5	17.841	0.0067	
30/0 N, A: 60/180 Hi F N	-8.4	17.841	0.0877	
30/0 N, A: 60/180 N	-5.925	17.841	0.2265	
30/0 N, A: Baseline	-1.7	17.841	0.7276	
30/0 N, Rest Mask	3.885	13.82	0.3053	
30/0 N, VoltHyp	-20.208	14.157	<.0001	S
60/180 E, 60/180 EPAP	-1.144	15.355	0.7852	
60/180 E, 60/180 HiFE	16.156			
60/180 E, 60/180 LoFE	-5.616	14.682	0.1642	
60/180 E, 60/180 N	-0.294	14.157	0.9394	
60/180 E, 60/180 PS	-9.994	14.157	0.0112	
60/180 E, 60/60 E	-2.211	13.734	0.5564	
60/180 E, A: 60/180 E	-8.294	17.508	0.0858	
60/180 E, A: 60/180 Hi F E	-10.669	17.508	0.0279	
60/180 E, A: 60/180 Hi F N	-5.569	17.508	0.2465	
60/180 E, A: 60/180 N	-3.094	17.508	0.5185	
60/180 E, A: Baseline	1.131	17.508	0.8133	
60/180 E, Rest Mask	6.716	13.386	0.0691	
60/180 E, VoltHyp	-17.378	13.734	<.0001	S
60/180 EPAP, 60/180 HiFE	17.3			
60/180 EPAP, 60/180 LoFE	-4.471	16.209	0.3144	

60/180 EPAP, 60/180 N	0.85	15.734	0.8434	
60/180 EPAP, 60/180 PS	-8.85	15.734	0.042	
60/180 EPAP, 60/60 E	-1.067	15.355	0.7995	
60/180 EPAP, A: 60/180 E	-7.15	18.806	0.1667	
60/180 EPAP, A: 60/180 Hi F E	-9.525	18.806	0.0666	
60/180 EPAP, A: 60/180 Hi F N	-4.425	18.806	0.3905	
60/180 EPAP, A: 60/180 N	-1.95	18.806	0.7047	
60/180 EPAP, A: Baseline	2.275	18.806	0.6584	
60/180 EPAP, Rest Mask	7.86	15.045	0.0586	
60/180 EPAP, VoltHyp	-16.233	15.355	0.0002	S
60/180 HiFE, 60/180 LoFE	-21.771	.	.	
60/180 HiFE, 60/180 N	-16.45	.	.	
60/180 HiFE, 60/180 PS	-26.15	.	.	
60/180 HiFE, 60/60 E	-18.367	.	.	
60/180 HiFE, A: 60/180 E	-24.45	.	.	
60/180 HiFE, A: 60/180 Hi F E	-26.825	.	.	
60/180 HiFE, A: 60/180 Hi F N	-21.725	.	.	
60/180 HiFE, A: 60/180 N	-19.25	.	.	
60/180 HiFE, A: Baseline	-15.025	.	.	
60/180 HiFE, Rest Mask	-9.44	.	.	
60/180 HiFE, VoltHyp	-33.533	.	.	
60/180 LoFE, 60/180 N	5.321	15.078	0.1989	
60/180 LoFE, 60/180 PS	-4.379	15.078	0.2898	
60/180 LoFE, 60/60 E	3.405	14.682	0.3974	
60/180 LoFE, A: 60/180 E	-2.679	18.261	0.592	
60/180 LoFE, A: 60/180 Hi F E	-5.054	18.261	0.3129	
60/180 LoFE, A: 60/180 Hi F N	0.046	18.261	0.9926	
60/180 LoFE, A: 60/180 N	2.521	18.261	0.6138	
60/180 LoFE, A: Baseline	6.746	18.261	0.1789	
60/180 LoFE, Rest Mask	12.331	14.358	0.0022	
60/180 LoFE, VoltHyp	-11.762	14.682	0.0042	
60/180 N, 60/180 PS	-9.7	14.567	0.0166	
60/180 N, 60/60 E	-1.917	14.157	0.6208	
60/180 N, A: 60/180 E	-8	17.841	0.1036	
60/180 N, A: 60/180 Hi F E	-10.375	17.841	0.0357	
60/180 N, A: 60/180 Hi F N	-5.275	17.841	0.2812	
60/180 N, A: 60/180 N	-2.8	17.841	0.5664	
60/180 N, A: Baseline	1.425	17.841	0.7703	
60/180 N, Rest Mask	7.01	13.82	0.0662	
60/180 N, VoltHyp	-17.083	14.157	<.0001	S
60/180 PS, 60/60 E	7.783	14.157	0.0468	
60/180 PS, A: 60/180 E	1.7	17.841	0.7276	
60/180 PS, A: 60/180 Hi F E	-0.675	17.841	0.89	
60/180 PS, A: 60/180 Hi F N	4.425	17.841	0.3655	
60/180 PS, A: 60/180 N	6.9	17.841	0.1596	
60/180 PS, A: Baseline	11.125	17.841	0.0246	
60/180 PS, Rest Mask	16.71	13.82	<.0001	S
60/180 PS, VoltHyp	-7.383	14.157	0.059	
60/60 E, A: 60/180 E	-6.083	17.508	0.2059	
60/60 E, A: 60/180 Hi F E	-8.458	17.508	0.0799	
60/60 E, A: 60/180 Hi F N	-3.358	17.508	0.4836	
60/60 E, A: 60/180 N	-0.883	17.508	0.8536	
60/60 E, A: Baseline	3.342	17.508	0.4858	
60/60 E, Rest Mask	8.927	13.386	0.0164	
60/60 E, VoltHyp	-15.167	13.734	0.0001	S
A: 60/180 E, A: 60/180 Hi F E	-2.375	20.601	0.6735	
A: 60/180 E, A: 60/180 Hi F N	2.725	20.601	0.6288	
A: 60/180 E, A: 60/180 N	5.2	20.601	0.3571	
A: 60/180 E, A: Baseline	9.425	20.601	0.0969	

A: 60/180 E, Rest Mask	15.01	17.236	0.0019	
A: 60/180 E, VoltHyp	-9.083	17.508	0.0603	
A: 60/180 Hi F E, A: 60/180 Hi F N	5.1	20.601	0.3664	
A: 60/180 Hi F E, A: 60/180 N	7.575	20.601	0.1809	
A: 60/180 Hi F E, A: Baseline	11.8	20.601	0.0385	
A: 60/180 Hi F E, Rest Mask	17.385	17.236	0.0004	S
A: 60/180 Hi F E, VoltHyp	-6.708	17.508	0.1634	
A: 60/180 Hi F N, A: 60/180 N	2.475	20.601	0.6606	
A: 60/180 Hi F N, A: Baseline	6.7	20.601	0.2361	
A: 60/180 Hi F N, Rest Mask	12.285	17.236	0.0105	
A: 60/180 Hi F N, VoltHyp	-11.808	17.508	0.0153	
A: 60/180 N, A: Baseline	4.225	20.601	0.454	
A: 60/180 N, Rest Mask	9.81	17.236	0.0397	
A: 60/180 N, VoltHyp	-14.283	17.508	0.0036	
A: Baseline, Rest Mask	5.585	17.236	0.2379	
A: Baseline, VoltHyp	-18.508	17.508	0.0002	S
Rest Mask, VoltHyp	-24.093	13.386	<.0001	S

Comparisons in this table are not significant unless the corresponding p-value is less than .0004.

56 cases were omitted due to missing values.



## ANOVA Table for [H+]

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	15	2999.988	199.999	6.449	<.0001
Residual	94	2915.351	31.014		

Model II estimate of between component variance: 24.846

50 cases were omitted due to missing values.

Bonferroni/Dunn for [H+]

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value	
30/0 E, 30/0 N	-7.236	9.668	0.0074	
30/0 E, 60/180 E	-0.218	9.115	0.9303	
30/0 E, 60/180 EPAP	-0.024	10.044	0.9931	
30/0 E, 60/180 HiFE	-4.428	15.787	0.3073	
30/0 E, 60/180 LoFE	1.915	9.365	0.4561	
30/0 E, 60/180 N	-7.861	9.668	0.0037	
30/0 E, 60/180 PS	4.496	9.365	0.0822	
30/0 E, 60/60 E	0.573	9.365	0.8234	
30/0 E, A: 60/180 E	0.571	12.058	0.8627	
30/0 E, A: 60/180 Hi F E	-1.595	12.058	0.6295	
30/0 E, A: 60/180 Hi F N	-12.948	12.058	0.0002	S
30/0 E, A: 60/180 N	-12.401	12.058	0.0003	S
30/0 E, A: Baseline	-11.683	13.417	0.002	
30/0 E, Rest Mask	-7.57	9.115	0.0031	
30/0 E, VoltHyp	3.736	9.365	0.1476	
30/0 N, 60/180 E	7.018	9.668	0.0093	
30/0 N, 60/180 EPAP	7.212	10.548	0.0141	
30/0 N, 60/180 HiFE	2.808	16.113	0.5251	
30/0 N, 60/180 LoFE	9.151	9.904	0.0011	
30/0 N, 60/180 N	-0.625	10.191	0.823	
30/0 N, 60/180 PS	11.732	9.904	<.0001	S
30/0 N, 60/60 E	7.809	9.904	0.0048	
30/0 N, A: 60/180 E	7.807	12.481	0.0243	
30/0 N, A: 60/180 Hi F E	5.641	12.481	0.1014	
30/0 N, A: 60/180 Hi F N	-5.712	12.481	0.0973	
30/0 N, A: 60/180 N	-5.165	12.481	0.1332	
30/0 N, A: Baseline	-4.447	13.798	0.2412	
30/0 N, Rest Mask	-0.333	9.668	0.8998	
30/0 N, VoltHyp	10.972	9.904	0.0001	S
60/180 E, 60/180 EPAP	0.194	10.044	0.9437	
60/180 E, 60/180 HiFE	-4.21	15.787	0.3316	
60/180 E, 60/180 LoFE	2.133	9.365	0.4066	
60/180 E, 60/180 N	-7.642	9.668	0.0047	
60/180 E, 60/180 PS	4.714	9.365	0.0686	
60/180 E, 60/60 E	0.791	9.365	0.7579	
60/180 E, A: 60/180 E	0.79	12.058	0.8111	
60/180 E, A: 60/180 Hi F E	-1.376	12.058	0.6771	
60/180 E, A: 60/180 Hi F N	-12.73	12.058	0.0002	S
60/180 E, A: 60/180 N	-12.183	12.058	0.0004	S
60/180 E, A: Baseline	-11.465	13.417	0.0023	
60/180 E, Rest Mask	-7.351	9.115	0.004	
60/180 E, VoltHyp	3.954	9.365	0.1256	
60/180 EPAP, 60/180 HiFE	-4.404	16.342	0.3265	
60/180 EPAP, 60/180 LoFE	1.939	10.271	0.4914	

60/180 EPAP, 60/180 N	-7.837	10.548	0.0078	
60/180 EPAP, 60/180 PS	4.52	10.271	0.1107	
60/180 EPAP, 60/60 E	0.597	10.271	0.8321	
60/180 EPAP, A: 60/180 E	0.595	12.775	0.865	
60/180 EPAP, A: 60/180 Hi F E	-1.571	12.775	0.6537	
60/180 EPAP, A: 60/180 Hi F N	-12.924	12.775	0.0004	S
60/180 EPAP, A: 60/180 N	-12.377	12.775	0.0006	
60/180 EPAP, A: Baseline	-11.659	14.065	0.0031	
60/180 EPAP, Rest Mask	-7.546	10.044	0.0072	
60/180 EPAP, VoltHyp	3.76	10.271	0.1836	
60/180 HiFE, 60/180 LoFE	6.343	15.933	0.1485	
60/180 HiFE, 60/180 N	-3.433	16.113	0.4375	
60/180 HiFE, 60/180 PS	8.924	15.933	0.0432	
60/180 HiFE, 60/60 E	5.001	15.933	0.2536	
60/180 HiFE, A: 60/180 E	4.999	17.651	0.3026	
60/180 HiFE, A: 60/180 Hi F E	2.833	17.651	0.5583	
60/180 HiFE, A: 60/180 Hi F N	-8.52	17.651	0.0805	
60/180 HiFE, A: 60/180 N	-7.973	17.651	0.1016	
60/180 HiFE, A: Baseline	-7.255	18.606	0.1569	
60/180 HiFE, Rest Mask	-3.142	15.787	0.4682	
60/180 HiFE, VoltHyp	8.164	15.933	0.0639	
60/180 LoFE, 60/180 N	-9.775	9.904	0.0005	
60/180 LoFE, 60/180 PS	2.581	9.608	0.3281	
60/180 LoFE, 60/60 E	-1.342	9.608	0.6104	
60/180 LoFE, A: 60/180 E	-1.344	12.248	0.689	
60/180 LoFE, A: 60/180 Hi F E	-3.509	12.248	0.297	
60/180 LoFE, A: 60/180 Hi F N	-14.863	12.248	<.0001	S
60/180 LoFE, A: 60/180 N	-14.316	12.248	<.0001	S
60/180 LoFE, A: Baseline	-13.598	13.588	0.0004	S
60/180 LoFE, Rest Mask	-9.484	9.365	0.0004	S
60/180 LoFE, VoltHyp	1.821	9.608	0.4895	
60/180 N, 60/180 PS	12.357	9.904	<.0001	S
60/180 N, 60/60 E	8.433	9.904	0.0024	
60/180 N, A: 60/180 E	8.432	12.481	0.0152	
60/180 N, A: 60/180 Hi F E	6.266	12.481	0.0693	
60/180 N, A: 60/180 Hi F N	-5.087	12.481	0.1391	
60/180 N, A: 60/180 N	-4.541	12.481	0.1863	
60/180 N, A: Baseline	-3.822	13.798	0.3133	
60/180 N, Rest Mask	0.291	9.668	0.9125	
60/180 N, VoltHyp	11.597	9.904	<.0001	S
60/180 PS, 60/60 E	-3.923	9.608	0.1384	
60/180 PS, A: 60/180 E	-3.925	12.248	0.2439	
60/180 PS, A: 60/180 Hi F E	-6.091	12.248	0.072	
60/180 PS, A: 60/180 Hi F N	-17.444	12.248	<.0001	S
60/180 PS, A: 60/180 N	-16.897	12.248	<.0001	S
60/180 PS, A: Baseline	-16.179	13.588	<.0001	S
60/180 PS, Rest Mask	-12.065	9.365	<.0001	S
60/180 PS, VoltHyp	-0.76	9.608	0.7729	
60/60 E, A: 60/180 E	-0.002	12.248	0.9996	
60/60 E, A: 60/180 Hi F E	-2.167	12.248	0.5188	
60/60 E, A: 60/180 Hi F N	-13.521	12.248	0.0001	S
60/60 E, A: 60/180 N	-12.974	12.248	0.0002	S
60/60 E, A: Baseline	-12.256	13.588	0.0014	
60/60 E, Rest Mask	-8.142	9.365	0.002	
60/60 E, VoltHyp	3.163	9.608	0.2312	
A: 60/180 E, A: 60/180 Hi F E	-2.166	14.412	0.5836	
A: 60/180 E, A: 60/180 Hi F N	-13.519	14.412	0.0009	
A: 60/180 E, A: 60/180 N	-12.972	14.412	0.0014	
A: 60/180 E, A: Baseline	-12.254	15.567	0.0049	

A: 60/180 E, Rest Mask	-8.141	12.058	0.0153	
A: 60/180 E, VoltHyp	3.165	12.248	0.3467	
A: 60/180 Hi F E, A: 60/180 Hi F N	-11.353	14.412	0.0049	
A: 60/180 Hi F E, A: 60/180 N	-10.806	14.412	0.0073	
A: 60/180 Hi F E, A: Baseline	-10.088	15.567	0.0197	
A: 60/180 Hi F E, Rest Mask	-5.975	12.058	0.073	
A: 60/180 Hi F E, VoltHyp	5.331	12.248	0.1145	
A: 60/180 Hi F N, A: 60/180 N	0.547	14.412	0.8898	
A: 60/180 Hi F N, A: Baseline	1.265	15.567	0.7668	
A: 60/180 Hi F N, Rest Mask	5.379	12.058	0.1059	
A: 60/180 Hi F N, VoltHyp	16.684	12.248	<.0001	S
A: 60/180 N, A: Baseline	0.718	15.567	0.8663	
A: 60/180 N, Rest Mask	4.832	12.058	0.1459	
A: 60/180 N, VoltHyp	16.137	12.248	<.0001	S
A: Baseline, Rest Mask	4.113	13.417	0.2647	
A: Baseline, VoltHyp	15.419	13.588	<.0001	S
Rest Mask, VoltHyp	11.306	9.365	<.0001	S

Comparisons in this table are not significant unless the corresponding p-value is less than .0004.

50 cases were omitted due to missing values.

## ANOVA Table for PaO2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	15	59911.315	3994.088	17.877	<.0001
Residual	93	20777.878	223.418		

Model II estimate of between component variance: 559.441

51 cases were omitted due to missing values.

Bonferroni/Dunn for PaO2

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value	
30/0 E, 30/0 N	-9.25	25.958	0.1952	
30/0 E, 60/180 E	-8.2	24.474	0.223	
30/0 E, 60/180 EPAP	-11	26.969	0.1387	
30/0 E, 60/180 HiFE	4.5	42.39	0.6984	
30/0 E, 60/180 LoFE	-9.5	25.958	0.1835	
30/0 E, 60/180 N	-11.75	25.958	0.1008	
30/0 E, 60/180 PS	-19.667	25.144	0.0052	
30/0 E, 60/60 E	-7.889	25.144	0.2536	
30/0 E, A: 60/180 E	53	32.376	<.0001	S
30/0 E, A: 60/180 Hi F E	54	32.376	<.0001	S
30/0 E, A: 60/180 Hi F N	42	32.376	<.0001	S
30/0 E, A: 60/180 N	41.5	32.376	<.0001	S
30/0 E, A: Baseline	-57.667	36.024	<.0001	S
30/0 E, Rest Mask	20	24.474	0.0035	
30/0 E, VoltHyp	-10.556	25.144	0.1277	
30/0 N, 60/180 E	1.05	25.958	0.8826	
30/0 N, 60/180 EPAP	-1.75	28.323	0.8215	
30/0 N, 60/180 HiFE	13.75	43.264	0.2476	
30/0 N, 60/180 LoFE	-0.25	27.362	0.9734	
30/0 N, 60/180 N	-2.5	27.362	0.7387	
30/0 N, 60/180 PS	-10.417	26.592	0.1549	
30/0 N, 60/60 E	1.361	26.592	0.8518	
30/0 N, A: 60/180 E	62.25	33.512	<.0001	S
30/0 N, A: 60/180 Hi F E	63.25	33.512	<.0001	S
30/0 N, A: 60/180 Hi F N	51.25	33.512	<.0001	S
30/0 N, A: 60/180 N	50.75	33.512	<.0001	S
30/0 N, A: Baseline	-48.417	37.049	<.0001	S
30/0 N, Rest Mask	29.25	25.958	<.0001	S
30/0 N, VoltHyp	-1.306	26.592	0.8577	
60/180 E, 60/180 EPAP	-2.8	26.969	0.7047	
60/180 E, 60/180 HiFE	12.7	42.39	0.2755	
60/180 E, 60/180 LoFE	-1.3	25.958	0.8549	
60/180 E, 60/180 N	-3.55	25.958	0.6178	
60/180 E, 60/180 PS	-11.467	25.144	0.0984	
60/180 E, 60/60 E	0.311	25.144	0.964	
60/180 E, A: 60/180 E	61.2	32.376	<.0001	S
60/180 E, A: 60/180 Hi F E	62.2	32.376	<.0001	S
60/180 E, A: 60/180 Hi F N	50.2	32.376	<.0001	S
60/180 E, A: 60/180 N	49.7	32.376	<.0001	S
60/180 E, A: Baseline	-49.467	36.024	<.0001	S
60/180 E, Rest Mask	28.2	24.474	<.0001	S
60/180 E, VoltHyp	-2.356	25.144	0.7324	
60/180 EPAP, 60/180 HiFE	15.5	43.878	0.1991	
60/180 EPAP, 60/180 LoFE	1.5	28.323	0.8467	

60/180 EPAP, 60/180 N	-0.75	28.323	0.923	
60/180 EPAP, 60/180 PS	-8.667	27.579	0.2529	
60/180 EPAP, 60/60 E	3.111	27.579	0.6805	
60/180 EPAP, A: 60/180 E	64	34.301	<.0001	S
60/180 EPAP, A: 60/180 Hi F E	65	34.301	<.0001	S
60/180 EPAP, A: 60/180 Hi F N	53	34.301	<.0001	S
60/180 EPAP, A: 60/180 N	52.5	34.301	<.0001	S
60/180 EPAP, A: Baseline	-46.667	37.764	<.0001	S
60/180 EPAP, Rest Mask	31	26.969	<.0001	S
60/180 EPAP, VoltHyp	0.444	27.579	0.9531	
60/180 HiFE, 60/180 LoFE	-14	43.264	0.2391	
60/180 HiFE, 60/180 N	-16.25	43.264	0.1724	
60/180 HiFE, 60/180 PS	-24.167	42.78	0.0414	
60/180 HiFE, 60/60 E	-12.389	42.78	0.2918	
60/180 HiFE, A: 60/180 E	48.5	47.393	0.0003	S
60/180 HiFE, A: 60/180 Hi F E	49.5	47.393	0.0002	S
60/180 HiFE, A: 60/180 Hi F N	37.5	47.393	0.0047	
60/180 HiFE, A: 60/180 N	37	47.393	0.0053	
60/180 HiFE, A: Baseline	-62.167	49.957	<.0001	S
60/180 HiFE, Rest Mask	15.5	42.39	0.1839	
60/180 HiFE, VoltHyp	-15.056	42.78	0.2008	
60/180 LoFE, 60/180 N	-2.25	27.362	0.764	
60/180 LoFE, 60/180 PS	-10.167	26.592	0.1649	
60/180 LoFE, 60/60 E	1.611	26.592	0.8249	
60/180 LoFE, A: 60/180 E	62.5	33.512	<.0001	S
60/180 LoFE, A: 60/180 Hi F E	63.5	33.512	<.0001	S
60/180 LoFE, A: 60/180 Hi F N	51.5	33.512	<.0001	S
60/180 LoFE, A: 60/180 N	51	33.512	<.0001	S
60/180 LoFE, A: Baseline	-48.167	37.049	<.0001	S
60/180 LoFE, Rest Mask	29.5	25.958	<.0001	S
60/180 LoFE, VoltHyp	-1.056	26.592	0.8848	
60/180 N, 60/180 PS	-7.917	26.592	0.2785	
60/180 N, 60/60 E	3.861	26.592	0.5963	
60/180 N, A: 60/180 E	64.75	33.512	<.0001	S
60/180 N, A: 60/180 Hi F E	65.75	33.512	<.0001	S
60/180 N, A: 60/180 Hi F N	53.75	33.512	<.0001	S
60/180 N, A: 60/180 N	53.25	33.512	<.0001	S
60/180 N, A: Baseline	-45.917	37.049	<.0001	S
60/180 N, Rest Mask	31.75	25.958	<.0001	S
60/180 N, VoltHyp	1.194	26.592	0.8697	
60/180 PS, 60/60 E	11.778	25.798	0.098	
60/180 PS, A: 60/180 E	72.667	32.886	<.0001	S
60/180 PS, A: 60/180 Hi F E	73.667	32.886	<.0001	S
60/180 PS, A: 60/180 Hi F N	61.667	32.886	<.0001	S
60/180 PS, A: 60/180 N	61.167	32.886	<.0001	S
60/180 PS, A: Baseline	-38	36.483	0.0002	S
60/180 PS, Rest Mask	39.667	25.144	<.0001	S
60/180 PS, VoltHyp	9.111	25.798	0.1992	
60/60 E, A: 60/180 E	60.889	32.886	<.0001	S
60/60 E, A: 60/180 Hi F E	61.889	32.886	<.0001	S
60/60 E, A: 60/180 Hi F N	49.889	32.886	<.0001	S
60/60 E, A: 60/180 N	49.389	32.886	<.0001	S
60/60 E, A: Baseline	-49.778	36.483	<.0001	S
60/60 E, Rest Mask	27.889	25.144	0.0001	S
60/60 E, VoltHyp	-2.667	25.798	0.706	
A: 60/180 E, A: 60/180 Hi F E	1	38.696	0.9248	
A: 60/180 E, A: 60/180 Hi F N	-11	38.696	0.3007	
A: 60/180 E, A: 60/180 N	-11.5	38.696	0.2794	
A: 60/180 E, A: Baseline	-110.667	41.797	<.0001	S

A: 60/180 E, Rest Mask	-33	32.376	0.0003	S
A: 60/180 E, VoltHyp	-63.556	32.886	<.0001	S
A: 60/180 Hi F E, A: 60/180 Hi F N	-12	38.696	0.2591	
A: 60/180 Hi F E, A: 60/180 N	-12.5	38.696	0.24	
A: 60/180 Hi F E, A: Baseline	-111.667	41.797	<.0001	S
A: 60/180 Hi F E, Rest Mask	-34	32.376	0.0002	S
A: 60/180 Hi F E, VoltHyp	-64.556	32.886	<.0001	S
A: 60/180 Hi F N, A: 60/180 N	-0.5	38.696	0.9624	
A: 60/180 Hi F N, A: Baseline	-99.667	41.797	<.0001	S
A: 60/180 Hi F N, Rest Mask	-22	32.376	0.0146	
A: 60/180 Hi F N, VoltHyp	-52.556	32.886	<.0001	S
A: 60/180 N, A: Baseline	-99.167	41.797	<.0001	S
A: 60/180 N, Rest Mask	-21.5	32.376	0.017	
A: 60/180 N, VoltHyp	-52.056	32.886	<.0001	S
A: Baseline, Rest Mask	77.667	36.024	<.0001	S
A: Baseline, VoltHyp	47.111	36.483	<.0001	S
Rest Mask, VoltHyp	-30.556	25.144	<.0001	S

Comparisons in this table are not significant unless the corresponding p-value is less than .0004.

51 cases were omitted due to missing values.

**ANOVA Table for PaCO<sub>2</sub>**

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	15	5675.677	378.378	5.76	<.0001
Residual	94	6174.971	65.691		

Model II estimate of between component variance: 45.975

50 cases were omitted due to missing values.

Bonferroni/Dunn for PaCO<sub>2</sub>

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value	
30/0 E, 30/0 N	-9.423	14.07	0.0161	
30/0 E, 60/180 E	0.11	13.265	0.9759	
30/0 E, 60/180 EPAP	-0.324	14.618	0.9355	
30/0 E, 60/180 HiFE	-5.16	22.976	0.4132	
30/0 E, 60/180 LoFE	1.946	13.629	0.6026	
30/0 E, 60/180 N	-11.823	14.07	0.0028	
30/0 E, 60/180 PS	6.534	13.629	0.0826	
30/0 E, 60/60 E	1.957	13.629	0.6005	
30/0 E, A: 60/180 E	3.165	17.549	0.5108	
30/0 E, A: 60/180 Hi F E	1.29	17.549	0.7885	
30/0 E, A: 60/180 Hi F N	-15.51	17.549	0.0017	
30/0 E, A: 60/180 N	-14.61	17.549	0.003	
30/0 E, A: Baseline	-14.91	19.526	0.0063	
30/0 E, Rest Mask	-11.84	13.265	0.0015	
30/0 E, VoltHyp	5.334	13.629	0.1553	
30/0 N, 60/180 E	9.533	14.07	0.0149	
30/0 N, 60/180 EPAP	9.098	15.352	0.0326	
30/0 N, 60/180 HiFE	4.263	23.45	0.5075	
30/0 N, 60/180 LoFE	11.368	14.413	0.0048	
30/0 N, 60/180 N	-2.4	14.831	0.5551	
30/0 N, 60/180 PS	15.957	14.413	0.0001	S
30/0 N, 60/60 E	11.379	14.413	0.0048	
30/0 N, A: 60/180 E	12.588	18.164	0.0129	
30/0 N, A: 60/180 Hi F E	10.713	18.164	0.0334	
30/0 N, A: 60/180 Hi F N	-6.087	18.164	0.2231	
30/0 N, A: 60/180 N	-5.188	18.164	0.2986	
30/0 N, A: Baseline	-5.487	20.082	0.3198	
30/0 N, Rest Mask	-2.418	14.07	0.531	
30/0 N, VoltHyp	14.757	14.413	0.0003	S
60/180 E, 60/180 EPAP	-0.434	14.618	0.9136	
60/180 E, 60/180 HiFE	-5.27	22.976	0.4034	
60/180 E, 60/180 LoFE	1.836	13.629	0.6232	
60/180 E, 60/180 N	-11.933	14.07	0.0025	
60/180 E, 60/180 PS	6.424	13.629	0.0878	
60/180 E, 60/60 E	1.847	13.629	0.6211	
60/180 E, A: 60/180 E	3.055	17.549	0.5256	
60/180 E, A: 60/180 Hi F E	1.18	17.549	0.8061	
60/180 E, A: 60/180 Hi F N	-15.62	17.549	0.0016	
60/180 E, A: 60/180 N	-14.72	17.549	0.0028	
60/180 E, A: Baseline	-15.02	19.526	0.0059	
60/180 E, Rest Mask	-11.95	13.265	0.0014	
60/180 E, VoltHyp	5.224	13.629	0.1639	
60/180 EPAP, 60/180 HiFE	-4.836	23.783	0.4587	
60/180 EPAP, 60/180 LoFE	2.27	14.948	0.5797	

60/180 EPAP, 60/180 N	-11.498	15.352	0.0073	
60/180 EPAP, 60/180 PS	6.859	14.948	0.0964	
60/180 EPAP, 60/60 E	2.281	14.948	0.5779	
60/180 EPAP, A: 60/180 E	3.489	18.592	0.4939	
60/180 EPAP, A: 60/180 Hi F E	1.614	18.592	0.7514	
60/180 EPAP, A: 60/180 Hi F N	-15.186	18.592	0.0036	
60/180 EPAP, A: 60/180 N	-14.286	18.592	0.006	
60/180 EPAP, A: Baseline	-14.586	20.469	0.0106	
60/180 EPAP, Rest Mask	-11.516	14.618	0.0049	
60/180 EPAP, VoltHyp	5.659	14.948	0.1692	
60/180 HiFE, 60/180 LoFE	7.106	23.188	0.2649	
60/180 HiFE, 60/180 N	-6.663	23.45	0.3011	
60/180 HiFE, 60/180 PS	11.694	23.188	0.0681	
60/180 HiFE, 60/60 E	7.117	23.188	0.2642	
60/180 HiFE, A: 60/180 E	8.325	25.688	0.2386	
60/180 HiFE, A: 60/180 Hi F E	6.45	25.688	0.3605	
60/180 HiFE, A: 60/180 Hi F N	-10.35	25.688	0.1437	
60/180 HiFE, A: 60/180 N	-9.45	25.688	0.1814	
60/180 HiFE, A: Baseline	-9.75	27.078	0.1908	
60/180 HiFE, Rest Mask	-6.68	22.976	0.29	
60/180 HiFE, VoltHyp	10.494	23.188	0.101	
60/180 LoFE, 60/180 N	-13.768	14.413	0.0007	
60/180 LoFE, 60/180 PS	4.589	13.983	0.2328	
60/180 LoFE, 60/60 E	0.011	13.983	0.9977	
60/180 LoFE, A: 60/180 E	1.219	17.825	0.8028	
60/180 LoFE, A: 60/180 Hi F E	-0.656	17.825	0.8932	
60/180 LoFE, A: 60/180 Hi F N	-17.456	17.825	0.0005	
60/180 LoFE, A: 60/180 N	-16.556	17.825	0.001	
60/180 LoFE, A: Baseline	-16.856	19.775	0.0024	
60/180 LoFE, Rest Mask	-13.786	13.629	0.0004	S
60/180 LoFE, VoltHyp	3.389	13.983	0.3774	
60/180 N, 60/180 PS	18.357	14.413	<.0001	S
60/180 N, 60/60 E	13.779	14.413	0.0007	
60/180 N, A: 60/180 E	14.988	18.164	0.0033	
60/180 N, A: 60/180 Hi F E	13.113	18.164	0.0097	
60/180 N, A: 60/180 Hi F N	-3.688	18.164	0.4594	
60/180 N, A: 60/180 N	-2.788	18.164	0.5757	
60/180 N, A: Baseline	-3.087	20.082	0.575	
60/180 N, Rest Mask	-0.018	14.07	0.9964	
60/180 N, VoltHyp	17.157	14.413	<.0001	S
60/180 PS, 60/60 E	-4.578	13.983	0.2339	
60/180 PS, A: 60/180 E	-3.369	17.825	0.4908	
60/180 PS, A: 60/180 Hi F E	-5.244	17.825	0.2843	
60/180 PS, A: 60/180 Hi F N	-22.044	17.825	<.0001	S
60/180 PS, A: 60/180 N	-21.144	17.825	<.0001	S
60/180 PS, A: Baseline	-21.444	19.775	0.0001	S
60/180 PS, Rest Mask	-18.374	13.629	<.0001	S
60/180 PS, VoltHyp	-1.2	13.983	0.7542	
60/60 E, A: 60/180 E	1.208	17.825	0.8046	
60/60 E, A: 60/180 Hi F E	-0.667	17.825	0.8914	
60/60 E, A: 60/180 Hi F N	-17.467	17.825	0.0005	
60/60 E, A: 60/180 N	-16.567	17.825	0.001	
60/60 E, A: Baseline	-16.867	19.775	0.0024	
60/60 E, Rest Mask	-13.797	13.629	0.0004	S
60/60 E, VoltHyp	3.378	13.983	0.3789	
A: 60/180 E, A: 60/180 Hi F E	-1.875	20.975	0.7443	
A: 60/180 E, A: 60/180 Hi F N	-18.675	20.975	0.0016	
A: 60/180 E, A: 60/180 N	-17.775	20.975	0.0025	
A: 60/180 E, A: Baseline	-18.075	22.655	0.0044	



A: 60/180 E, Rest Mask	-15.005	17.549	0.0023	
A: 60/180 E, VoltHyp	2.169	17.825	0.657	
A: 60/180 Hi F E, A: 60/180 Hi F N	-16.8	20.975	0.0042	
A: 60/180 Hi F E, A: 60/180 N	-15.9	20.975	0.0067	
A: 60/180 Hi F E, A: Baseline	-16.2	22.655	0.0103	
A: 60/180 Hi F E, Rest Mask	-13.13	17.549	0.0074	
A: 60/180 Hi F E, VoltHyp	4.044	17.825	0.4084	
A: 60/180 Hi F N, A: 60/180 N	0.9	20.975	0.8756	
A: 60/180 Hi F N, A: Baseline	0.6	22.655	0.923	
A: 60/180 Hi F N, Rest Mask	3.67	17.549	0.446	
A: 60/180 Hi F N, VoltHyp	20.844	17.825	<.0001	S
A: 60/180 N, A: Baseline	-0.3	22.655	0.9615	
A: 60/180 N, Rest Mask	2.77	17.549	0.5649	
A: 60/180 N, VoltHyp	19.944	17.825	<.0001	S
A: Baseline, Rest Mask	3.07	19.526	0.5664	
A: Baseline, VoltHyp	20.244	19.775	0.0003	S
Rest Mask, VoltHyp	17.174	13.629	<.0001	S

Comparisons in this table are not significant unless the corresponding p-value is less than .0004.

50 cases were omitted due to missing values.

ANOVA Table for Mean PA Pressure

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	3	67.916	22.639	0.991	0.4298
Residual	12	273.999	22.833		

Model II estimate of between component variance: •  
3 cases were omitted due to missing values.

Bonferroni/Dunn for Mean PA Pressure

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value
A: 60/180 E, A: 60/180 Hi F E	0.477	11.584	0.89
A: 60/180 E, A: 60/180 Hi F N	3.81	11.584	0.2815
A: 60/180 E, A: 60/180 N	-1.91	11.584	0.5823
A: 60/180 E, A: Baseline	64.97	.	.
A: 60/180 Hi F E, A: 60/180 Hi F N	3.333	11.584	0.3435
A: 60/180 Hi F E, A: 60/180 N	-2.387	11.584	0.4933
A: 60/180 Hi F E, A: Baseline	64.493	.	.
A: 60/180 Hi F N, A: 60/180 N	-5.72	11.584	0.1163
A: 60/180 Hi F N, A: Baseline	61.16	.	.
A: 60/180 N, A: Baseline	66.88	.	.

Comparisons in this table are not significant unless the  
corresponding p-value is less than .005.  
3 cases were omitted due to missing values.

## ANOVA Table for PvO2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	4	387.934	96.984	8.292	0.0012
Residual	14	163.75	11.696		

Model II estimate of between component variance: 22.506

Bonferroni/Dunn for PvO2

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value	
A: 60/180 E, A: 60/180 Hi F E	-0.5	8.043	0.8392	
A: 60/180 E, A: 60/180 Hi F N	-7	8.043	0.0118	
A: 60/180 E, A: 60/180 N	-5.25	8.043	0.0476	
A: 60/180 E, A: Baseline	-13	8.687	0.0002	S
A: 60/180 Hi F E, A: 60/180 Hi F N	-6.5	8.043	0.0177	
A: 60/180 Hi F E, A: 60/180 N	-4.75	8.043	0.0697	
A: 60/180 Hi F E, A: Baseline	-12.5	8.687	0.0003	S
A: 60/180 Hi F N, A: 60/180 N	1.75	8.043	0.4812	
A: 60/180 Hi F N, A: Baseline	-6	8.687	0.0376	
A: 60/180 N, A: Baseline	-7.75	8.687	0.0102	

Comparisons in this table are not significant unless the corresponding p-value is less than .005.

ANOVA Table for SvO2 (IL)

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	3	26.157	8.719	0.28	0.839
Residual	12	374.048	31.171		

Model II estimate of between component variance: •  
3 cases were omitted due to missing values.

Bonferroni/Dunn for SvO2 (IL)  
Effect: Condition  
Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value
A: 60/180 E, A: 60/180 Hi F E	1.225	13.535	0.7617
A: 60/180 E, A: 60/180 Hi F N	-1.725	13.535	0.6699
A: 60/180 E, A: 60/180 N	1.525	13.535	0.706
A: 60/180 E, A: Baseline	71.075	.	.
A: 60/180 Hi F E, A: 60/180 Hi F N	-2.95	13.535	0.4693
A: 60/180 Hi F E, A: 60/180 N	0.3	13.535	0.9407
A: 60/180 Hi F E, A: Baseline	69.85	.	.
A: 60/180 Hi F N, A: 60/180 N	3.25	13.535	0.4264
A: 60/180 Hi F N, A: Baseline	72.8	.	.
A: 60/180 N, A: Baseline	69.55	.	.

Comparisons in this table are not significant unless the  
corresponding p-value is less than .005.  
3 cases were omitted due to missing values.

**ANOVA Table for PvCO<sub>2</sub>**

	DF	Sum of Squares	Mean Square	F-Value	P-Value
<b>Condition</b>	4	1110.005	277.501	13.525	0.0001
<b>Residual</b>	14	287.242	20.517		

Model II estimate of between component variance: 67.815

Bonferroni/Dunn for PvCO<sub>2</sub>

Effect: Condition

Significance Level: 5 %

<b>Paired Comparison</b>	<b>Mean Diff.</b>	<b>Crit. Diff</b>	<b>P-Value</b>	
A: 60/180 E, A: 60/180 Hi F E	-3.625	10.652	0.2767	
A: 60/180 E, A: 60/180 Hi F N	-17.725	10.652	<.0001	S
A: 60/180 E, A: 60/180 N	-16.8	10.652	0.0001	S
A: 60/180 E, A: Baseline	-16.633	11.505	0.0003	S
A: 60/180 Hi F E, A: 60/180 Hi F N	-14.1	10.652	0.0006	S
A: 60/180 Hi F E, A: 60/180 N	-13.175	10.652	0.0011	S
A: 60/180 Hi F E, A: Baseline	-13.008	11.505	0.0021	S
A: 60/180 Hi F N, A: 60/180 N	0.925	10.652	0.777	
A: 60/180 Hi F N, A: Baseline	1.092	11.505	0.757	
A: 60/180 N, A: Baseline	0.167	11.505	0.9623	

Comparisons in this table are not significant unless the corresponding p-value is less than .005.

ANOVA Table for CO

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Condition	3	1.323	0.441	0.59	0.6332
Residual	12	8.973	0.748		

Model II estimate of between component variance: •  
3 cases were omitted due to missing values.

Bonferroni/Dunn for CO

Effect: Condition

Significance Level: 5 %

Paired Comparison	Mean Diff.	Crit. Diff	P-Value
A: 60/180 E, A: 60/180 Hi F E	0.16	2.096	0.7975
A: 60/180 E, A: 60/180 Hi F N	-0.354	2.096	0.5732
A: 60/180 E, A: 60/180 N	0.442	2.096	0.4839
A: 60/180 E, A: Baseline	6.05	.	.
A: 60/180 Hi F E, A: 60/180 Hi F N	-0.515	2.096	0.4165
A: 60/180 Hi F E, A: 60/180 N	0.281	2.096	0.6538
A: 60/180 Hi F E, A: Baseline	5.89	.	.
A: 60/180 Hi F N, A: 60/180 N	0.796	2.096	0.2175
A: 60/180 Hi F N, A: Baseline	6.404	.	.
A: 60/180 N, A: Baseline	5.608	.	.

Comparisons in this table are not significant unless the  
corresponding p-value is less than .005.  
3 cases were omitted due to missing values.

## **Conclusions:**

Cardiovascular function during PPB to 60 mmHg is well maintained with the full coverage ATAGS G-suit. Mean arterial blood pressure, although not statistically significant, tended to be greater with a 3:1 ratio of G-suit to mask pressure when compared to a 1:1 ratio. The phasic ventilatory interventions utilized in this study, while hypothesized to improve venous return to the heart, did not provide any added benefit to maintenance of cardiovascular function when compared to the usual 60 mmHg PPB with lower extremity G-suit inflation pressure of 180 mmHg.

All modes of ventilatory support for this study incorporated a high baseline PPB or CPAP in order to maintain alveolar oxygen tensions at acceptable levels. This resulted in a mean increase in intrathoracic pressure and a consequent reduction in venous return. The effects on cardiac output, ie. preload, afterload, contractility and heart rate depend on both the baseline cardiovascular status as well as the specific mode of phasic ventilation used. It was hypothesized that the decreased venous return caused by high levels of PPB would be less during an inspiratory pressure support pattern of ventilation (Figure 2) where inspiratory effort is augmented by the ventilator. Expiratory pressure support was predicted to worsen the cardiovascular status by further reductions in venous return and cardiac output. The finding of no significant change over baseline 60 mmHg PPB using these modes of ventilation suggests that the degree of cardiovascular depression caused by increases in mean airway pressure are well compensated for by the full coverage G-suit inflated to 180 mmHg. It is possible that for higher mean airway pressures, the degree of venous return gained by the G-suit could be improved by ventilatory interventions.

Hyperventilation as defined by hypocapnia is known to occur with PPB to 60 mmHg. High frequency oscillatory ventilation has been shown clinically to result in hypoventilation and hypercapnia. However, the addition of high frequency ventilation to baseline PPB of 60 mmHg did not obliterate the tendency of experienced volunteers to hyperventilate. Mean  $\text{PaCO}_2$  during all eucapneic oscillatory interventions was 24 mmHg vs. 39-40 mmHg during resting controls.  $\text{PaCO}_2$  during PPB with superimposed oscillation was not statistically different from non-oscillatory interventions.

The correlation of  $\text{PaCO}_2$  reduction and poorer cognitive function indicates that either the reduction in blood flow and brain blood volume from hyperventilation or anxiety stimulating hyperventilation (e.g., fear, stress, etc.) is reducing cognitive performance. The comparisons of all eucapnic runs and normocapnic runs yield differences which are not statistically significant due to the wide variations in performance. Normalization of  $\text{PaCO}_2$  by the addition of carbon dioxide to the breathing gas may have beneficial effects on pilot performance as predicted by the neurocognitive test battery administered in this study.

As predicted by the alveolar gas equation, addition of  $\text{CO}_2$  to the breathing gas did result in increased  $\text{PaCO}_2$  and an improvement in  $\text{PaO}_2$ . This is seen as a trend at sea level and significant at 24,000 ft. The addition of  $\text{CO}_2$  to improve altitude hypoxia could provide an additional means of pilot protection without placing the pilot at worsening risk of cardiovascular collapse and barotrauma from even greater levels of PPB. The of improvement in neurocognitive performance at higher  $\text{PaCO}_2$  as described above was not due to increased  $\text{PaO}_2$ .

The beneficial effects of normocapnia during neurocognitive performance with PPB of 60 mmHg have been demonstrated at 24,900 ft. simulated altitude while simulating the  $\text{PaO}_2$  that would be expected at 50,000 ft. breathing 100% oxygen. The mechanism of this improvement could be related to enhancements of cerebral blood flow and/or improved arterial oxygen tension and need to be further investigated. Only after better understanding the mechanisms of impaired neurocognitive function at altitude can we provide countermeasures. These can be achieved by either avoiding the well known reflex hyperventilation of PPB and/or by the addition of carbon dioxide to the breathing gas. The present invasive studies have demonstrated that the use of respiratory rate as a method of training pilots to avoid hyperventilation during PPB is not predictive of degree of hypocapnia.  $\text{P}_{\text{ET}}\text{CO}_2$  also has been shown to be an unreliable predictor of  $\text{PaCO}_2$  at altitude during PPB. Further invasive studies are needed to evaluate cerebral blood flow, oxygen delivery and performance as a function of actual  $\text{PaCO}_2$ .

## **Summary**

- (1) Phasic pressure support with greater pressure during expiration (EPAP) was intolerable to subjects because of an extremely high work of breathing. Phasic pressure support during inspiration tended to increase minute ventilation, and lower arterial  $\text{PCO}_2$  compared with conventional PPB.
- (2) Oscillatory pressure changes superimposed upon constant PPB using the COMBAT EDGE did not reflexly inhibit the usually observed involuntary hyperventilation. Hypocapnia could be avoided by adding  $\text{CO}_2$  to the inspired gas.
- (3) Hypocapnia induced by involuntary hyperventilation did impair psychomotor performance when arterial  $\text{PCO}_2$  values fell below 20 mmHg. There was no effect of arterial  $\text{PO}_2$  on the measures of performance used in this study.
- (4) There was a significant difference between end-tidal and arterial  $\text{PCO}_2$ , with end-tidal values tending to underestimate arterial  $\text{CO}_2$  tension by up to 25 mmHg. The slope of the line of least squares regression is 0.88.



- (5) Hypoxia and impairment of psychomotor performance due to hypocapnia during PPB at a simulated altitude of 50,000 ft (24,900 ft chamber altitude, 34% O<sub>2</sub>) can be prevented by the addition of CO<sub>2</sub> to the breathing gas.

Table 3: Calculated  $P_{AO_2}$  as function of  $F_{IO_2}$ ,  $P_ACO_2$  and RQ at altitude without inspired  $CO_2$ , no PPB

Altitude	$P_m$	$P_b$	$F_{IO_2}$	$F_{ICO_2}$	$P_{ICO_2}$	$P_{atmO_2}$	$P_{iO_2}$	$P_{ACO_2}$	RQ	$P_{AO_2}$
feet	mmHg	mmHg			mmHg	mmHg	mmHg	mmHg		mmHg
25,000	0	282	0.30	0	0	85	71	40	1.0	30.5
									0	
25,000	0	282	0.31	0	0	87	73	40	1.0	32.9
									0	
25,000	0	282	0.32	0	0	90	75	40	1.0	35.2
									0	
25,000	0	282	0.33	0	0	93	78	40	1.0	37.6
									0	
25,000	0	282	0.34	0	0	96	80	40	1.0	39.9
									0	
25,000	0	282	0.35	0	0	99	82	40	1.0	42.3
									0	
25,000	0	282	0.30	0	0	85	71	40	1.6	41.0
									0	
25,000	0	282	0.31	0	0	87	73	40	1.6	43.2
									0	
25,000	0	282	0.32	0	0	90	75	40	1.6	45.4
									0	
25,000	0	282	0.33	0	0	93	78	40	1.6	47.6
									0	
25,000	0	282	0.34	0	0	96	80	40	1.6	49.8
									0	
25,000	0	282	0.35	0	0	99	82	40	1.6	52.0
									0	
25,000	0	282	0.30	0	0	85	71	20	1.0	50.5
									0	
25,000	0	282	0.31	0	0	87	73	20	1.0	52.9
									0	
25,000	0	282	0.32	0	0	90	75	20	1.0	55.2
									0	
25,000	0	282	0.33	0	0	93	78	20	1.0	57.6
									0	
25,000	0	282	0.34	0	0	96	80	20	1.0	59.9
									0	
25,000	0	282	0.35	0	0	99	82	20	1.0	62.3
									0	
25,000	0	282	0.30	0	0	85	71	20	1.6	55.8
									0	
25,000	0	282	0.31	0	0	87	73	20	1.6	58.0
									0	
25,000	0	282	0.32	0	0	90	75	20	1.6	60.3
									0	

25,000	0	282	0.33	0	0	93	78	20	1.6	62.6
									0	
25,000	0	282	0.34	0	0	96	80	20	1.6	64.9
									0	
25,000	0	282	0.34	0	0	96	80	20	1.6	64.9
									0	
50,000	0	87.3	1.00	0	0	87	40	40	1.0	0.3
									0	
50,000	0	87.3	1.00	0	0	87	40	40	1.6	0.3
									0	
50,000	0	87.3	1.00	0	0	87	40	20	1.0	20.3
									0	
50,000	0	87.3	1.00	0	0	87	40	20	1.6	20.3
									0	

Table 4: Calculated  $P_{AO_2}$  as function of  $F_{IO_2}$ ,  $P_ACO_2$  and RQ without inspired  $CO_2$  at altitude, 60 mmHg PPB

Altitude	$P_m$	$P_b$	$F_{IO_2}$	$F_{ICO_2}$	$P_{ICO_2}$	$P_{atmO_2}$	$P_{iO_2}$	$P_{ACO_2}$	RQ	$P_{AO_2}$
feet	mmHg	mmHg			mmHg	mmHg	mmHg	mmHg		mmHg
25,000	60	342	0.30	0	0	103	89	40	1.0	48.5
									0	
25,000	60	342	0.31	0	0	106	92	40	1.0	51.5
									0	
25,000	60	342	0.32	0	0	109	94	40	1.0	54.4
									0	
25,000	60	342	0.33	0	0	113	97	40	1.0	57.4
									0	
25,000	60	342	0.34	0	0	116	100	40	1.0	60.3
									0	
25,000	60	342	0.35	0	0	120	103	40	1.0	63.3
									0	
25,000	60	342	0.30	0	0	103	89	40	1.6	59.0
									0	
25,000	60	342	0.31	0	0	106	92	40	1.6	61.8
									0	
25,000	60	342	0.32	0	0	109	94	40	1.6	64.6
									0	
25,000	60	342	0.33	0	0	113	97	40	1.6	67.4
									0	
25,000	60	342	0.34	0	0	116	100	40	1.6	70.2
									0	
25,000	60	342	0.35	0	0	120	103	40	1.6	73.0
									0	
25,000	60	342	0.30	0	0	103	89	20	1.0	68.5
									0	
25,000	60	342	0.31	0	0	106	92	20	1.0	71.5
									0	
25,000	60	342	0.32	0	0	109	94	20	1.0	74.4
									0	
25,000	60	342	0.33	0	0	113	97	20	1.0	77.4
									0	
25,000	60	342	0.34	0	0	116	100	20	1.0	80.3
									0	
25,000	60	342	0.35	0	0	120	103	20	1.0	83.3
									0	
25,000	60	342	0.30	0	0	103	89	20	1.6	73.8
									0	
25,000	60	342	0.31	0	0	106	92	20	1.6	76.6
									0	
25,000	60	342	0.32	0	0	109	94	20	1.6	79.5
									0	

25,000	60	342	0.33	0	0	113	97	20	1.6	82.4
									0	
25,000	60	342	0.34	0	0	116	100	20	1.6	85.3
									0	
25,000	60	342	0.35	0	0	120	103	20	1.6	88.1
									0	
50,000	60	147	1.00	0	0	147	100	40	1.0	60.3
									0	
50,000	60	147	1.00	0	0	147	100	40	1.6	60.3
									0	
50,000	60	147	1.00	0	0	147	100	20	1.0	80.3
									0	
50,000	60	147	1.00	0	0	147	100	20	1.6	80.3
									0	

Table 5: Calculated  $P_{AO_2}$  as function of  $F_{IO_2}$ ,  $P_{ACO_2}$  and RQ with 5% inspired  $CO_2$  at altitude, no PPB

Altitude	$P_m$	$P_b$	$F_{IO_2}$	$F_{ICO_2}$	$P_{ICO_2}$	$P_{atmO_2}$	$P_{iO_2}$	$P_{ACO_2}$	RQ	$P_{AO_2}$
feet	mmHg	mmHg			mmHg	mmHg <sup>2</sup>	mmHg	mmHg		mmHg
25,000	0	282	0.30	0.05	11.75	85	71	40	1.00	42.3
25,000	0	282	0.31	0.05	11.75	87	73	40	1.00	32.9
25,000	0	282	0.32	0.05	11.75	90	75	40	1.00	35.2
25,000	0	282	0.33	0.05	11.75	93	78	40	1.00	37.6
25,000	0	282	0.34	0.05	11.75	96	80	40	1.00	39.9
25,000	0	282	0.35	0.05	11.75	99	82	40	1.00	42.3
25,000	0	282	0.30	0.05	11.75	85	71	40	1.60	41.0
25,000	0	282	0.31	0.05	11.75	87	73	40	1.60	43.2
25,000	0	282	0.32	0.05	11.75	90	75	40	1.60	45.4
25,000	0	282	0.33	0.05	11.75	93	78	40	1.60	47.6
25,000	0	282	0.34	0.05	11.75	96	80	40	1.60	49.8
25,000	0	282	0.35	0.05	11.75	99	82	40	1.60	52.0
25,000	0	282	0.30	0.05	11.75	85	71	20	1.00	50.5
25,000	0	282	0.31	0.05	11.75	87	73	20	1.00	52.9
25,000	0	282	0.32	0.05	11.75	90	75	20	1.00	55.2
25,000	0	282	0.33	0.05	11.75	93	78	20	1.00	57.6
25,000	0	282	0.34	0.05	11.75	96	80	20	1.00	59.9
25,000	0	282	0.35	0.05	11.75	99	82	20	1.00	62.3
25,000	0	282	0.30	0.05	11.75	85	71	20	1.60	55.8
25,000	0	282	0.31	0.05	11.75	87	73	20	1.60	58.0
25,000	0	282	0.32	0.05	11.75	90	75	20	1.60	60.3
25,000	0	282	0.33	0.05	11.75	93	78	20	1.60	62.6
25,000	0	282	0.34	0.05	11.75	96	80	20	1.60	64.9
25,000	0	282	0.34	0.05	11.75	96	80	20	1.60	64.9
50,000	0	87.3	1.00	0.05	2.02	87	40	40	1.00	0.3
50,000	0	87.3	1.00	0.05	2.02	87	40	40	1.60	0.3
50,000	0	87.3	1.00	0.05	2.02	87	40	20	1.00	20.3
50,000	0	87.3	1.00	0.05	2.02	87	40	20	1.60	20.3

Table 6: Calculated  $P_{A}O_2$  as function of  $F_{I}O_2$ ,  $P_{A}CO_2$  and RQ with 5% inspired  $CO_2$  at altitude, 60 mmHg PPB

Altitude	$P_m$	$P_b$	$F_{I}O_2$	$F_{I}CO_2$	$P_{i}CO_2$	$P_{atm}O$	$P_{i}O_2$	$P_{A}CO_2$	RQ	$P_{A}O_2$
feet	mmHg	mmHg			mmHg	mmHg	mmHg	mmHg		mmHg
25,000	60	342	0.30	0.05	14.75	103	89	40	1.00	48.5
25,000	60	342	0.31	0.05	14.75	106	92	40	1.00	51.5
25,000	60	342	0.32	0.05	14.75	109	94	40	1.00	54.4
25,000	60	342	0.33	0.05	14.75	113	97	40	1.00	57.4
25,000	60	342	0.34	0.05	14.75	116	100	40	1.00	60.3
25,000	60	342	0.35	0.05	14.75	120	103	40	1.00	63.3
25,000	60	342	0.30	0.05	14.75	103	89	40	1.60	59.0
25,000	60	342	0.31	0.05	14.75	106	92	40	1.60	61.8
25,000	60	342	0.32	0.05	14.75	109	94	40	1.60	64.6
25,000	60	342	0.33	0.05	14.75	113	97	40	1.60	67.4
25,000	60	342	0.34	0.05	14.75	116	100	40	1.60	70.2
25,000	60	342	0.35	0.05	14.75	120	103	40	1.60	73.0
25,000	60	342	0.30	0.05	14.75	103	89	20	1.00	68.5
25,000	60	342	0.31	0.05	14.75	106	92	20	1.00	71.5
25,000	60	342	0.32	0.05	14.75	109	94	20	1.00	74.4
25,000	60	342	0.33	0.05	14.75	113	97	20	1.00	77.4
25,000	60	342	0.34	0.05	14.75	116	100	20	1.00	80.3
25,000	60	342	0.35	0.05	14.75	120	103	20	1.00	83.3
25,000	60	342	0.30	0.05	14.75	103	89	20	1.60	73.8
25,000	60	342	0.31	0.05	14.75	106	92	20	1.60	76.6
25,000	60	342	0.32	0.05	14.75	109	94	20	1.60	79.5
25,000	60	342	0.33	0.05	14.75	113	97	20	1.60	82.4
25,000	60	342	0.34	0.05	14.75	116	100	20	1.60	85.3
25,000	60	342	0.35	0.05	14.75	120	103	20	1.60	88.1
50,000	60	147	1.00	0.05	5.02	147	100	40	1.00	60.3
50,000	60	147	1.00	0.05	5.02	147	100	40	1.60	60.3
50,000	60	147	1.00	0.05	5.02	147	100	20	1.00	80.3
50,000	60	147	1.00	0.05	5.02	147	100	20	1.60	80.3

Table 7: Calculated  $P_{A}O_2$  as function of  $F_{I}O_2$ ,  $P_{A}CO_2$  and RQ with 10% inspired  $CO_2$  at altitude, no PPB

Altitude feet	$P_m$ mmHg	$P_b$ mmHg	$F_{I}O_2$	$F_{I}CO_2$	$P_{i}CO_2$ mmHg	$P_{atm}O_2$ mmHg	$P_{i}O_2$ mmHg	$P_{A}CO_2$ mmHg	RQ	$P_{A}O_2$ mmHg
25,000	0	282	0.30	0.1	23.5	85	71	40	1.00	54.0
25,000	0	282	0.31	0.1	23.5	87	73	40	1.00	32.9
25,000	0	282	0.32	0.1	23.5	90	75	40	1.00	35.2
25,000	0	282	0.33	0.1	23.5	93	78	40	1.00	37.6
25,000	0	282	0.34	0.1	23.5	96	80	40	1.00	39.9
25,000	0	282	0.35	0.1	23.5	99	82	40	1.00	42.3
25,000	0	282	0.30	0.1	23.5	85	71	40	1.60	41.0
25,000	0	282	0.31	0.1	23.5	87	73	40	1.60	43.2
25,000	0	282	0.32	0.1	23.5	90	75	40	1.60	45.4
25,000	0	282	0.33	0.1	23.5	93	78	40	1.60	47.6
25,000	0	282	0.34	0.1	23.5	96	80	40	1.60	49.8
25,000	0	282	0.35	0.1	23.5	99	82	40	1.60	52.0
25,000	0	282	0.30	0.1	23.5	85	71	20	1.00	50.5
25,000	0	282	0.31	0.1	23.5	87	73	20	1.00	52.9
25,000	0	282	0.32	0.1	23.5	90	75	20	1.00	55.2
25,000	0	282	0.33	0.1	23.5	93	78	20	1.00	57.6
25,000	0	282	0.34	0.1	23.5	96	80	20	1.00	59.9
25,000	0	282	0.35	0.1	23.5	99	82	20	1.00	62.3
25,000	0	282	0.30	0.1	23.5	85	71	20	1.60	55.8
25,000	0	282	0.31	0.1	23.5	87	73	20	1.60	58.0
25,000	0	282	0.32	0.1	23.5	90	75	20	1.60	60.3
25,000	0	282	0.33	0.1	23.5	93	78	20	1.60	62.6
25,000	0	282	0.34	0.1	23.5	96	80	20	1.60	64.9
25,000	0	282	0.34	0.1	23.5	96	80	20	1.60	64.9
50,000	0	87.3	1.00	0.1	4.03	87	40	40	1.00	0.3
50,000	0	87.3	1.00	0.1	4.03	87	40	40	1.60	0.3
50,000	0	87.3	1.00	0.1	4.03	87	40	20	1.00	20.3
50,000	0	87.3	1.00	0.1	4.03	87	40	20	1.60	20.3



Table 8: Calculated  $P_{AO_2}$  as function of  $F_{IO_2}$ ,  $P_ACO_2$  and RQ with 10% inspired  $CO_2$  at altitude, 60 mmHg PPB

Altitude	$P_m$	$P_b$	$F_{IO_2}$	$F_{ICO_2}$	$P_{ICO_2}$	$P_{atmO}$	$P_{iO_2}$	$P_{ACO_2}$	RQ	$P_{AO_2}$
feet	mmHg	mmHg			mmHg	mmHg	mmHg	mmHg		mmHg
25,000	60	342	0.30	0.1	29.5	103	89	40	1.00	48.5
25,000	60	342	0.31	0.1	29.5	106	92	40	1.00	51.5
25,000	60	342	0.32	0.1	29.5	109	94	40	1.00	54.4
25,000	60	342	0.33	0.1	29.5	113	97	40	1.00	57.4
25,000	60	342	0.34	0.1	29.5	116	100	40	1.00	60.3
25,000	60	342	0.35	0.1	29.5	120	103	40	1.00	63.3
25,000	60	342	0.30	0.1	29.5	103	89	40	1.60	59.0
25,000	60	342	0.31	0.1	29.5	106	92	40	1.60	61.8
25,000	60	342	0.32	0.1	29.5	109	94	40	1.60	64.6
25,000	60	342	0.33	0.1	29.5	113	97	40	1.60	67.4
25,000	60	342	0.34	0.1	29.5	116	100	40	1.60	70.2
25,000	60	342	0.35	0.1	29.5	120	103	40	1.60	73.0
25,000	60	342	0.30	0.1	29.5	103	89	20	1.00	68.5
25,000	60	342	0.31	0.1	29.5	106	92	20	1.00	71.5
25,000	60	342	0.32	0.1	29.5	109	94	20	1.00	74.4
25,000	60	342	0.33	0.1	29.5	113	97	20	1.00	77.4
25,000	60	342	0.34	0.1	29.5	116	100	20	1.00	80.3
25,000	60	342	0.35	0.1	29.5	120	103	20	1.00	83.3
25,000	60	342	0.30	0.1	29.5	103	89	20	1.60	73.8
25,000	60	342	0.31	0.1	29.5	106	92	20	1.60	76.6
25,000	60	342	0.32	0.1	29.5	109	94	20	1.60	79.5
25,000	60	342	0.33	0.1	29.5	113	97	20	1.60	82.4
25,000	60	342	0.34	0.1	29.5	116	100	20	1.60	85.3
25,000	60	342	0.35	0.1	29.5	120	103	20	1.60	88.1
50,000	60	147	1.00	0.1	10.03	147	100	40	1.00	60.3
50,000	60	147	1.00	0.1	10.03	147	100	40	1.60	60.3
50,000	60	147	1.00	0.1	10.03	147	100	20	1.00	80.3
50,000	60	147	1.00	0.1	10.03	147	100	20	1.60	80.3

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